THE famhp TIMES

Annual Report 2015

Recognition on a European level for famhp's expertise

Oncology

After earning its stripes in oncology, in 2014, as a result of its positive assessment of Lynparza (a treatment for ovarian cancer), famhp continued in the same vein in 2015. The work performed by the Belgian experts on the Cotellic and Lenvima dossiers led to a marketing authorisation and new options for the treatment of melanomas and thyroid cancers respectively. In the meantime, famhp has been appointed as the rapporteur for a number of new oncological medicinal products.

Vaccines

With regard to vaccines, famhp has been actively involved on a European level in the assessment of all requests made for new vaccines (Gardasil 9 – used to prevent for example cervical cancer, Mosquirix – the first vaccine against malaria and Vaxelis – a vaccine which protects against diphtheria, tetanus, whooping cough, hepatitis B, poliomyelitis and invasive infections such as pneumonia and meningitis) which have received a positive opinion from the EMA's (European Medicines Agency) CHMP (Committee for Medicinal Products for Human Use).

initiatives to promote the development of priority medicines and early access to medicines for certain patients. PRIME (PRIority MEdicines) is a process monitored closely in the framework of the early access to medicines initiatives, as discussed within the European Commission's working group.

During CHMP's meeting held in December 2015, professor Koen Norga, paediatric oncologist at university of Antwerp and vice-president of PDCO (Paediatric Committee) within EMA, was appointed as a co-opted member of CHMP. In this capacity he provides a link with the Paediatric Investigation Plans or PIP examined by PDCO.

Endocrinology

In endocrinology, famhp's experts were co-responsible, as rapporteur, for the successful assessment of Kanuma, used in cases of rare congenital diseases affecting fat metabolism.

Moreover, the Belgian delegation to CHMP was also actively involved in EMA's

ProCost: a pilot project to enhance the value of our services

Famhp plays an essential role in protecting public health and finances this critical mission by charging for the dossiers it handles. In this way, the funding received from the State, and thus directly from tax payers, can be kept at a very low level compared with other public service organisations. This arrangement can continue over the long term as long as it remains equitable. However, most of the agency's costs for services have not significantly changed for a quarter of a century. The operators in the sector who pay for our services have raised questions over whether our tariffs remain equitable. To answer this question, a project has been set up to improve our understanding of the cost of our activities: ProCost. Its principle is very simple: whenever an individual starts an activity, he/she enters this in the ProCost application (simply by clicking on the activity concerned). The system itself then performs the necessary calculations.

By recording the time spent by every member of our organisation on each of our activities, we can determine a fair price for what we produce for the benefit of public health.

Moreover, ProCost will prove to be a useful tool for every user, since this system gives a better indication of the relative importance of each of the activities he/she is required to perform. It is an extremely valuable self-management tool which individuals can use to help them achieve their annual targets.

A FEW WORDS FROM THE CHIEF EXECUTIVE OFFICER

A fascinating year, that's the very least you can say about 2015

It was our first full year under the auspices of Minister Maggie De Block. As always, famhp was committed to providing the Minister with willing support to ensure the successful delivery of the Public Health policy. You can read an interview with Minister De Block later on in this journal, however, I can tell you that, starting from when she took up her appointment, numerous projects where famhp wanted to and could make a difference were waiting for our attention.

Providing patients with faster access to new and promising medicines, implementing new legislation on clinical trials, preventing resistance to antibiotics, implementing new legislation on medicines for veterinary use, combatting counterfeit medicines and other illegal medicines, developing our expertise in the medical devices sector etc. In 2015, famhp achieved significant progress in a number of areas.

In fact, all our efforts tend towards a single objective: to provide the best possible support for patients.
I would like to thank everyone at famhp for their contribution to achieving this objective. I would also like to thank our partners and political leaders. Indeed, it is only by working together that we can move forward.

Our annual report

Summarising our activities and results for the year is a titanic task.
The deliberations on certain dossiers, the nuances which we have attempted to introduce, the motivation behind certain decisions ... it is not easy to express in a simple table or administrative document the long journey which we have taken to achieve each result.

Yet nonetheless, presenting our results continues to be a privilege which I value greatly. I am proud of what famhp achieved last year. This is why we have once again tried to present our results in a way which will make them interesting to discover. We have thus collated into a journal the accomplishments which we are keen to highlight, to make you aware that our agency handles subjects which are very important in your daily life.

This year also, we have produced a second volume which details our agency's results in facts and figures. We have attempted to present them to you in a more accessible way via charts and graphics which, we hope, will say more than an endless series of numbers.

We hope you enjoy reading about us.

Xavier De Cuyper
Chief Executive Officer

Contents

An interview with Maggie De Block,
Minister of Social Affairs and Public Health

Minister De Block, one of the main objectives of the federal government's agreement was to guarantee that the healthcare received by all Belgian citizens would be compatible with the evolving needs of the patient. Do you think that significant milestones on the path to this objective were reached in 2015?

The key principle of my policy, as Minister of Public Health, is that the patient should occupy a central position. The challenge is to offer the citizens of Belgium the highest possible quality of healthcare, in keeping with current requirements. At the same time, we must ensure the overall accessibility and long-term future of the system. Access to this care must be available to everyone, today and in the future. It is inconceivable to envisage that new therapies might only be available to the most wealthy members of our society. We must target our investments so as to ensure the long-term future of our system based on solidarity.

"The Pact for the Future has allowed us to make a significant step forwards."

To achieve these objectives, we must engage in an in-depth restructuring of this system. This is a long-term endeavour, for which I have adopted a step-by-step approach which involves working closely with all the parties concerned. And this approach is paying dividends: in 2015, we achieved significant progress. Patients now have access to innovative medicines and the price which they have to pay for certain medicines is falling. Other examples I could mention are: the increases to the budget for unmet medical needs, the maximisation of the "patent cliff" phenomenon, whereby the price of a medicine drops sharply as soon as it is no longer patent protected, the "prescribe cheaper medicines" campaign etc.

In Belgium, the patients, who you consider as your core concern, are less likely to willingly choose generic medicines compared with patients in other countries. Do you think that the use of generic medicines should be encouraged?

Patients need to feel confident that the medicines they take offer quality, safety and efficacy. As a result of the efforts of famhp and the pharmaceutical industry, they can indeed feel confident. In this respect, a generic medicinal product is just the same as a brand-name one. For me, these quality, safety and efficacy criteria are an overriding concern. I do not therefore have a preference for generic or brand-name medicines. However, it is important for me to ensure that the Belgian population is correctly informed: the prejudices sometimes associated with generic medicines are unfounded. Every medicine sold in a pharmacy can be trusted.

In Belgium, we fortunately have very few problems with the regulated distribution circuit. However, in 2015 we witnessed the increasing popularity of the illegal sale of medicines over the Internet. Does this trend worry you?

I should clarify that I am not, in principle, opposed to attempts to online initiatives. However, the prerequisite is that sufficient guarantees must be in place regarding quality and safety, both for patients and for prescribing healthcare professionals.

In Belgium, only pharmacists who operate a "bricks and mortar" retail pharmacy can also offer online pharmacy services. Moreover, European regulations oblige them to display on their website a logo consisting of a white cross on a green background and the Belgian flag. Belgian legislation also restricts the products they can sell on their webshop to over-the-counter medicines only. This arrangement offers better protection for patients, since when they need a prescription-only medicine they can benefit from the expert advice provided by the pharmacist. As an authority, we cannot guarantee the quality, safety and efficacy of medicines sold over the Internet via distribution circuits which are not regulated. Individuals who purchase a medicine in this way are taking two significant risks: not only are they endangering their health, but they could also be guilty of a crime if an illegal parcel is intercepted en route to their home. And this is happening with increasing frequency, thanks to the effective sharing of information between customs services and famhp's experts. I would appeal therefore to everyone to give their medication the respect it deserves and not to take medicines before they have consulted a pharmacist and, if necessary, a medical doctor. It's in their best interest to do so!

Finally, of which accomplishment achieved in 2015 are you most proud?

I'm very pleased that we truly managed to implement a patient-centred approach in all our projects. I say "we" because this would never have been possible without the full cooperation from my departments, various public services and, naturally, individuals working in the field. This is proof for me of everyone's willingness to reform our healthcare services for the benefit of patients. In hospitals, mental health units, frontline service, etc.

This willingness is also apparent in the pharmaceutical sector. The best example of this is undoubtedly the Pact for the Future for the patient, which we agreed with the pharmaceutical industry on 27 July 2015. Its objective is clear: we want to offer patients better and quicker access to advanced therapies. To achieve this, we are simplifying, for example, certain administrative procedures and are thus reducing the lead times for handling dossiers. We are in negotiation with other countries on the price of medicines intended for patients suffering from rare diseases. We are putting in place a stable climate of confidence for the pharmaceutical industry in Belgium, which will allow it to optimise the planning of its investments in R&D and will give patients the opportunity to benefit from innovative treatments. We are also introducing greater transparency, via deontological agreements with the sector, e.g. publishing the results of research work whose findings are negative, etc.
This is a truly unique agreement, which is increasingly attracting attention from outside Belgium.

Less than one year after signing the Pact, we have already observed the first results. In 2015, the pharmaceutical industry invested 5.5 % more in R&D in Belgium compared with 2014. And this year, two major players in the international healthcare sector have announced significant investment in the Belgian pharmaceutical sector. This is clearly good news for employment in this sector, as well as for patients who shall have faster access to innovation.

Thank you very much for this interview, Mrs De Block.

The counterfeiting of medicines driven by the cult of performance and appearance

DG INSPECTION's Special Investigation Unit works closely with customs services, notably with those which check parcels sent by post. Many of these parcels are intercepted because they contain illegal medicines, originating primarily from developing countries. In most cases, the contents of these parcels were ordered on illegal websites.

Posted parcels containing illegal medicines, as seized from carriers.

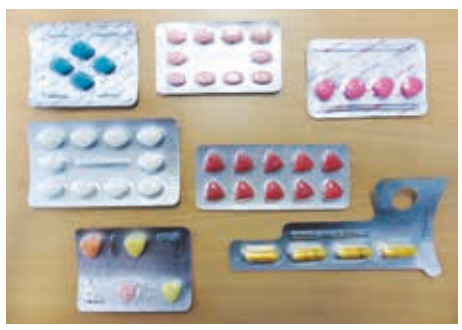
There are many types of illegal medicine, however, the most popular medicines for men are clearly those which treat erectile dysfunction and those designed to enhance athletic performance. For women, the most popular medicines are weight-loss products, fast-tanning products or, for women from North Africa, skin-lightening products.

From inefficacy to toxicity: caution, danger

Illegal medicines may contain no active substance. Sometimes the expected substances are present, but not always at the correct dosage. In some cases, the illegal medicines contain derivatives of the original substances whose effect is uncertain, and sometimes they even contain substances not included in the original composition of the medicine. It is a mixed picture, with a bit of everything. From this uncertainty stem the dangers associated with these medicines, for which there are no guarantees as to their composition. In addition to the problem of active substances, the medicines may, unfortunately, also contain impurities which are potentially toxic for vital organs such as the liver, kidneys and pancreas.

For men ...

The most prevalent illegal medicines in terms of volume intercepted are those which treat erectile dysfunction. Although these medicines commonly contain the three authorised active substances, sildenafil, tadalafil and vardenafil, they also frequently contain derivatives of these three substances.



These illegal tablets are produced in various shapes and colours, with the blister packs also not lacking in originality. These products are all presented as a treatment for erectile dysfunction.

To enhance athletic performance, the most popular substances are corticosteroids, in the form of tablets or injections, and hormones. These products are taken to increase muscle mass and physical strength and to promote the depletion of fat from muscles. They also increase appetite, growth and stimulate the bone marrow, which increases the production of red blood cells and boosts athletic performance. In the illegal market, these products are used at massive doses, which bear no relation to the recommended doses for legal therapeutic use.

The intensive use over the long term of these substances exposes the individual to a number of health risks: hypertension (high blood pressure), an increase in the level of "bad" cholesterol and a reduction in the level of "good" cholesterol, a higher risk of cardiovascular disease or coronary heart disease, a change to the structure of the heart (causing hypertension, arrhythmia, congestive heart failure, heart attack and sudden death) and severe lesions of the liver, especially with the oral forms. These fraudulent products can also promote male breast enlargement (gynecomastia), reduce sexual performance and cause temporary effects such as sterility and testicular atrophy.

Illegal anabolic steroids in the form of tablets or injections.

With injectable medicines, the additional danger is that they are not always sterile; as revealed by laboratory reports on numerous occasions. This exposes the consumer to the risk of septicaemia, the consequences of which can be catastrophic.
Despite the consequential adverse reactions, it is unfortunately fairly unrealistic to think that the public health message will be heard within the illegal distribution circuit, due to the overriding importance of athletic performance objectives among those involved.

... and for women

The Special Investigation Unit's inspectors and controllers often intercept weight-loss products, primarily those containing sibutramine, which are very popular among women. Moreover, there are typically two peak periods for the ordering of these products: at the end of the year before the festive period and in June before the summer holidays.

Note that EMA (European Medicines Agency) withdrew this medicine from the market in 2010 since it found that its benefits did not outweigh its risks. Taking sibutramine is linked to an increased risk of serious cardiovascular complications, such as heart attack or stroke. Moreover, the use of sibutramine can cause a blood clotting disorder, sudden muscular contractions, kidney and liver disorders and other serious adverse reactions.

Botanical Slimming and Slimex are two very well-known illegal medicines which contain sibutramine.

Sibutramine causes other adverse reactions, including intestinal occlusion, increased heart rate, hypertension and higher levels of anxiety. Furthermore, serious adverse reactions may occur when sibutramine is taken concurrently with other medicines.

Another substance whose consumption has increased over the last few years is the hormone, Melanotan II™. Also called "Barbie Drug", this injectable substance has hormonal effects, such as tanning the skin in thirty days. Known as MT-2, Melanotan II™ is not authorised in the European Union or in the United States of America. Consequently, any acquisition of this product is fraudulent. More and more people are taking it due to its "power" to accelerate tanning, as well as to reduce appetite and stimulate the libido. There are a number of dangers associated with this "miracle cocktail". This synthetic peptide, developed in the United States of America in the 1980's, is the synthetic version of a naturally-occurring hormone, α-MSH (alpha-Melanocyte-Stimulating Hormone).

Unlabelled bottles, removed from the illegal distribution circuit, analysis of which revealed the presence of Melanotan II.

This synthetic analogue acts for a much longer period of time than the naturally-occurring hormone.
The most well-known effect of Melanotan II™ is its effect on skin colour, determined by the production of melanin, the pigment responsible for tanning. The mean physiological plasma concentration of the natural hormone α-MSH is 25 ng/l, whereas the concentration of the synthetic hormone contained in Melanotan II™ is estimated to be between 5 and 25 mg/l, or between 5,000,000 and 25,000,000 times more concentrated than the natural hormone. These high concentrations make it easy to understand the potentially adverse effects on the body.

In addition to its use by women, Melanotan II™ is also used in bodybuilding for competitions in which appearance is also of prime importance.

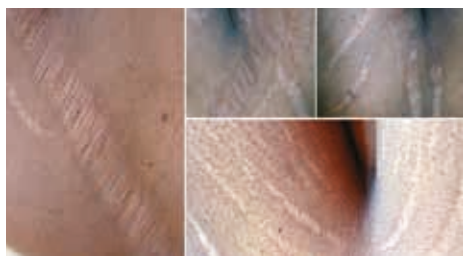
Skin whitening at any cost

Corticosteroid-based creams are one example of the illegal medicines found in many African shops in all urban centres in Belgium. Their "promise"? To whiten skin. Primarily used by women, they are generally applied to the face.

Tubes of cream containing corticosteroids, found in large quantities in African shops in all the large Belgian towns and cities, and also very frequently intercepted by customs.

Customs checks of cargo or luggage arriving from African countries results in the interception of thousands of tubes. This is a cultural problem which is particularly difficult to combat, even though it has consequences on public health.

The photos below bear witness to the effects caused by these creams: scars which, ultimately, become permanent. It has also been reported that parents apply these creams to their young children; a practice which is even more dangerous.



Skin damage caused by the excessive use of corticosteroids over the long term.

A blind and worrying trust

Somewhat surprisingly, intercepted illegal medicines cast a light on a society which gives performance and appearance absolute priority, preferring to ignore the consequences on health. This is, however, a paradox since, once the patients have suffered damage to their health, they turn for help to their medical doctor, pharmacist and medicines in the regulated distribution circuit.

The most prevalent illegal medicines in terms of volume intercepted are those which treat erectile dysfunction.

A new format for manufacturing and distribution authorisations for medicines

As a prerequisite for conducting their activities, manufacturers and distributors of medicinal products are required to hold an authorisation granted by famhp. For dozens of years, the Belgian authorisations adhered to a format which, in recent years, has proved to be no longer suited to the increasing complexity of the activities involved in the manufacturing and distribution of medicinal products.

Moreover, in 2007, EMA (European Medicines Agency) established a European format for manufacturing authorisations, called MIA (Manufacturing and Importation Authorisation). These authorisations describe the authorised manufacturing activities for which inspection has established that the holder complies with GMP (Good Manufacturing Practices).

More recently, a European format for distribution authorisations has also been created by EMA: the Wholesale-Distributors-Authorisation (WDA). This form describes the authorised distribution activities performed by the distributor for which inspection has established that GDP (Good Distribution Practices) are applied.

As a result of the creation of these two European authorisation formats, famhp was required to deliver two formats to manufacturers and distributors of medicinal products: the Belgian authorisation format and EMA's European authorisation format, which is better suited to the modern mode of operation of manufacturers and distributors of medicinal products. This duplication was clearly irrational. For this reason, and to simplify the situation, famhp now delivers a single authorisation format to manufacturers and distributors, which covers the manufacturing and distribution authorisations as established by EMA.

International standardisation and online accessibility

In addition to the administrative simplification introduced by the adoption of the European format for authorisations, this decision is justified by the many other benefits it brings. This standardisation means that the European formats are identical for every country in EEA (the European Economic Area), i.e. 31 countries (the 28 countries of the European Union plus Iceland, Liechtenstein and Norway) which use the same authorisation format. The manufacturing and distribution authorisations are also published online by the 31 competent authorities in the EudraGMDP (Good Manufacturing and Distribution Practices) database of the European Union. With no restrictions on access, this website lets any interested person check the activities which a manufacturer or distributor of medicinal products is authorised to perform. And to ensure rapid official confirmation of the granting of an authorisation, the authorisation is published online prior to the document being sent by post.

Advantages of the new format for manufacturing and distribution authorisations:

- simplification in terms of administrative management;
- more precise description of the authorised activities;
- adequacy of the format with the current reality;
- an identical format throughout the EEA;
- authorisations accessible online via the EudraGMDP website (www.eudragmdp.ema.europa.eu);
- faster availability of authorisations.

Authorisation in three parts

In practical terms, the authorisation format as it is now established in Belgium consists of three parts. Page one covers general information about the holder of the authorisation. Appended to this first page are the manufacturing/distribution authorisations (MIA and WDA), established in accordance with the format prescribed by EMA. The manufacturing authorisation (MIA) indicates, for each manufacturing site, the specific activities authorised; and the distribution authorisation (WDA) provides information about the distribution activities for which authorisation has been granted. Specific details regarding the categories of medicinal products (medical gases, radiopharmaceutical medicines, etc.) or the conditions under which the medicines concerned are stored complete the distribution information.

Based on the first year of use, famhp is very pleased to have adopted a new manufacturing and distribution authorisation format. The format is suited to the current status of the pharmaceutical sector and meets the expectations of all the European authorities in relation to health. The absence of complaints about abandoning the previous format and the requests from some holders for the option to benefit as quickly as possible from the new format confirm that famhp made the right decision!

To simplify the situation, famhp now delivers a single authorisation format to manufacturers and distributors, which covers the manufacturing and distribution authorisations as established by EMA.

PLATO: what's that?

PLATO, short for Planning Tool, is a centralised tool designed to help inspectors plan the various aspects of their internal and external tasks.

Which tasks does it facilitate?

The Retail Pharmacies Entity of the Dispensing Division was selected as the pilot entity to trial the first version of PLATO. This pilot phase highlighted two requirements: the need for a module for the inspector and another module for the coordinator or head of division.

The inspector's module consists of a data-entry interface and a report manager. PLATO's data-entry interface offers the inspector the following functionalities:

- initiate and/or schedule the inspection of a pharmacy;
- manage the activities performed in relation to the inspection (including the inspection report);
- record investigations requested by a third party, such as legal assistance or following-up the taking of samples;
- record tasks performed which do not relate to the inspection, such as administrative duties, training, conferences;
- enter the expenses incurred for each activity or based on a daily rate;
- work on the application in offline mode, e.g. via access to the inspection data for certain selected pharmacies. The tool then synchronises with the central database.

The report manager offers the inspector the option to generate various reports, such as a monthly report of all the activities performed by the inspector over a given period of time.

The PLATO application coordinator's module lets the coordinator:

- generate the overall report of inspection activities (inspection statistics);
- manage the various types of inspection by adding, amending or removing.

Modular design

PLATO has been developed as a modular tool to facilitate its extension into the Dispensing Division's other entities, such as Hospital Pharmacies/Medicinal Stocks at Healthcare Professionals Entity and and Medicinal stocks at Veterinarians Entity.

Moreover, there is nothing to prevent PLATO from being rolled-out to DG INSPECTION's other divisions.

And there is an additional advantage: PLATO has been designed to be compatible with the system of auto control at a lower cost.

The role of OMCL Net in combatting illegal pharmaceutical practices

The European Commission and the Council of Europe decided on 26 May 1994 to create a network of official medicines control laboratories called OMCL Net. This opened up a new opportunity for cooperative working in the field of testing the quality of medicines for human and veterinary use.

Sharing data and saving time

In the context of illegal pharmaceutical practices, two of OMCL Net's objectives are particularly important: mutual recognition, within the European Union, of tests carried out by official labs at the national level and improved communications among OMCLs via a network, handbooks and suitable IT tools. For example, the network's database is used on a daily basis by DG INSPECTION's Special Investigation Unit. Its utility derives from the fact that the results of analysis work on counterfeit medicines and on other illegal medicines are shared on a platform which can be accessed by health authorities from anywhere within the network. The database provides them with up-to-date information about the actual composition of counterfeit medicines and of other illegal medicines discovered by European colleagues, and thus prevents the duplication of tests that other laboratories might already have carried out.

A sharing system such as this promotes vigilance with regard to new products and allows product to be seized without systematically having to repeat expensive tests when they are not necessary. The overall outcome is higher levels of expertise and the fostering of a culture of information pooling.

Information Exchange of Counterfeit/Illegal Medicines in the OMCL Network

Part 1. Organisation details

Competent Authority/OMCL	Spanish Agency of Medicines and Medical Devices, Biological Products and Biotechnology Division. (OMCL-ES_AEMPS-B)
Contact Person	XXXXXX
Telephone N° (Include National Code)	XXXXXX
E-Mail Address	XXXXXX

Part 2. Product Details

Laboratory Reference Number	XXXXXX
Product Origin i.e. Internet, Legal/Illegal Market etc	ILLEGAL MARKET
Product Name	Human Growth Hormone 10 IU
Labelled Active Ingredient	Recombinant Human Growth Hormone
Licensed/Unlicensed	Unlicensed
Product Type	Illegal product
Dosage form (tablet, capsule, etc.)	Powder for solution for injection
Strength per unit dose	10 IU
Pack size	1 box of 10 vials and ampoules of solvent
MAHolder/Manufacturer (Where Appropriate)	
Distributor (If Different)	unknown
Batch Number	20130128
Expiry Date	01/2016
Rapid alert reference number	None
Summary of Problem or Deficiency i.e. Provide details of analysis results. Include Illegal actives identified If reporting counterfeit products provide information on packaging livery and any visual identifiers and any results obtained on authentic comparators	10 vials were provided by the Judicial Police to the Inspection and Control Department of the Spanish Medicines and Medical Devices Agency. The samples were collected in XXXXX Analysis performed: Sterility test. Results: Microbiological contamination was found.

Detail of Analytical Method Used i.e. HPLC, Column type, Mobile phase and Detection system. Info regarding availability of reference materials	Sterility test was performed following European Pharmacopoeia 8 th Edition 2.6.1 The test was performed on the 10 vials. The suitability test could not be performed because the number of vials was insufficient.
Further actions taken by the OMCL	The sterility test did not comply. *Paenibacillus spp., Staphylococcus epidermidis, Staphylococcus pasteuri* were isolated and identified. Report sent to our enforcement department

Insert Photographs of products and any relevant images of chromatograms/spectra etc

A report shared via OMCL Net contains details about the product, the context in which it was discovered, the test results and photos of the medicine concerned. These photos are very useful in assisting the visual identification of counterfeit medicines and of other illegal medicines in the field. A report of this type may also describe a sterility test on injectable products.

OMCL Net is a successful example of cooperation and the sharing of information between countries.

Rapid Alert System

Moreover, the collaborative platform also offers access to the Rapid Alerts issued by WGEO (Working Group of Enforcement Officers) set up by HMA (Heads of Medicines Agencies). WGEO comprises inspectors from the various health authorities, customs and police officers within the Member States of the European Union and its work focuses on combating illegal pharmaceutical practices. This system of alerts has made it possible to pool the reports, and ends the situation whereby some reports were sent out by e-mail while others were made available via the platform. This pooling process simplifies the searches for counterfeit medicines and other illegal medicines which have already been analysed. Moreover, the results of these analyses can be a cause for concern.

OMCL Net is a successful example of cooperation and the sharing of information between countries. Cooperation is without doubt critical in the fight against illegal pharmaceutical practices, and is an asset which all the participating countries now recognise.

Inspection of the manufacturers of medical devices: first impressions

Since the restructuring of DG INSPECTION at the end of 2014, the Industry Division has a team of three inspectors competent to perform inspections at the premises of the manufacturers of Class I, IIa, IIb, and III medical devices, and at the premises of people who received a delegation of power from the respective manufacturers of medical devices on European level and at the premises of the notified bodies.

In the past, these operators were inspected on an occasional basis, primarily to follow up complaints or reports. However, we can confirm that, in 2015, the first measures were taken towards implementing proactive inspections of this sector.

From January to November 2015, famhp inspected 25 manufacturers of medical devices and 2 people who received a delegation of power from a manufacturer of medical devices on European level Ten of these inspections were routine inspections, 2 were performed to follow up on an earlier inspection and 13 were prompted by a complaint or a report, or by a request from the Materiovigilance Cell or by an issue being noted by a colleague from another famhp department. Moreover, in the context of the various dossiers, famhp inspectors collaborated with their counterparts in the Netherlands, Luxembourg and France. This was a very rewarding experience for everyone involved.

During these inspections, two critical non-conformities were observed which led to the immediate withdrawal from sale of the products. 22 significant non-conformities and 42 other non-conformities were also found.

The inspections at the premises of manufacturers of Class I medical devices led to the detection of a higher number of non-conformities compared with the number of non-conformities detected at the premises of manufacturers of Class IIa, IIb and III devices. This demonstrates, according to famhp's experts, that it is also essential to inspect these manufacturers regularly, even though their products belong to a class characterised by a low degree of risk.

This first year of inspections revealed that an exhaustive list of manufacturers of medical devices (and of their critical subcontractors) should be compiled urgently. This list would enable more targeted inspections to be scheduled for the operators involved, based on a more sophisticated risk analysis.

A new single point of contact: logistiek@fagg-afmps.be, the logical choice!

To ensure that all the requests received are followed-up, Logistics has set up a single and central contact email address: logistiek@fagg-afmps.be. An automated process creates a "call" which initiates the automatic follow-up of each request, even when it has to be transferred to a different member of logistics staff, or to a particular group. This system ensures that no request is overlooked!

Simplified communication

From now on, a single request can trigger a set of actions. Previously, a request for catering, for a PC or for a replacement projector bulb might require several emails sent to different addresses, this is no longer the case!

Inspection of Good Manufacturing Practices in third countries

The pharmaceutical industry has not been able to avoid the phenomenon of globalisation and the problems stemming from it.

It is not unusual for pharmaceutical companies to source starting materials or Active Pharmaceutical Ingredients (API) from, or to subcontract all or some of the manufacture of a medicinal product to, countries in which overheads are lower, such as India, China or Indonesia. Some pharmaceutical companies have subsidiaries based outside the European Union or in a country with which no partnership agreements have been set up with the European Union. These subsidiaries may be responsible for the production of API, biotech medicines, or production intermediates on which the final processing is performed in the European Union prior to delivery to pharmacies.

Essential quality standards

Regardless of the situation, the issue of production quality criteria for these medicines is the same. The European standards in this field are called Good Manufacturing Practices (GMP)*. They are the only standards legally applicable and recognised in the European Union. Other countries apply national standards, such as the American competent authority, FDA's (Food and Drug Administration) GMP in the United States of America, or standards specific to a particular region of the world, e.g. the Far East GMP guidelines.

Consequently, from a pharmaceutical point of view, the world is divided into three zones:

- the member states of EEA (European Economic Area) which apply GMP;
- the countries which have entered into a Mutual Recognition Agreement (MRA) with Europe (Australia, Canada, New Zealand, Switzerland, Japan, Israel) and whose quality standards and inspection bodies have officially been recognised as being equivalent to European standards;
- the rest of the world, including the United States of America and Brazil, hereinafter referred to as third countries.

In the first two zones defined above, the inspections performed and the GMP certificates delivered by the competent authorities are mutually recognised between the countries. For example, medicines manufactured in Canada do not need to be analysed again before being allowed to enter the EEA.

GMP inspections outside the European Union

However, API and medicines originating from countries which have not entered into a mutual recognition agreement with the European Union must be inspected before entering EEA. A GMP inspection must then be conducted by the competent European authorities to ensure that these products meet the European standards.

For medicines which have been granted a Marketing Authorisation (MA) via a centralised procedure, the European Medicines Agency (EMA) coordinates the inspections. In most cases, the competent authorities which perform the inspection are those to which the European company responsible for marketing the product is accountable. Consider, for example, a medicine manufactured partly in the United States of Amercia by the American subsidiary of a pharmaceutical company, but which is released in Belgium by the Belgian parent company, and is distributed in the Netherlands, France and Germany. In this case, EMA asks the Belgian, Dutch, French or German authorities to make inspectors available to check the manufacturing steps in USA. The inspectors check the plant in which the medicines are manufactured, the personnel employed, management etc. The analytical control tests, contracts and consistency with the MA are also checked. If the subsidiary satisfies the requirements, the inspectors write up a positive report and a European GMP certificate is issued and placed in a European database available to the public called Eudra GMP. This document certifies that the European standards have been met by the American firm, and is valid throughout all the member states. Other European countries do not then have to inspect this company. The certificates are valid for three years. When a certificate expires, a new inspection is scheduled by EMA.

In the meantime, the American subsidiary may have been inspected by FDA. However, since there is no provision for mutual recognition, this inspection would not be valid in the European Union since it was not performed by European authorities. The converse is also true.

The cost of an absence of recognition

The duplication of inspections by FDA and EMA clearly has a high cost in terms of expense and non-productive worktime. Negotiations around the TTIP (Transatlantic Trade and Investment Partnership) have understandably sought to include pharmaceutical products and to set up mutual recognition. Other countries are currently negotiating with Europe to obtain similar recognition.

These various mutual recognition agreements shall ultimately streamline the workload for the inspection bodies and reduce the costs for pharmaceutical companies. These resources could then be redirected: by the authorities at problematic issues and by the pharmaceutical industry at development activities.

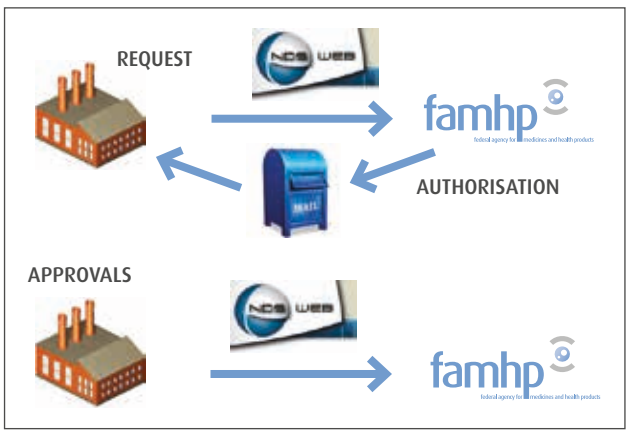
** Volume 4 of Eudralex*

NDS-web app speeds up the delivery of import and export authorisations

In 2014, DG INSPECTION's Narcotics Team launched the NDS-web application, a platform via which applications can be submitted for import and export authorisations for narcotics and psychotropic substances.

Using this application, the demands submitted are passed on directly to NDS (National Drugs control System) software, developed by UNODC (United Nations Office on Drugs and Crime) and used by famhp since 2012.

This provides a valuable alternative to paper-based applications, which can be lost. The new system offers guaranteed reception and more rapid handling. The holder of an authorisation for narcotics or psychotropic substances, or the pharmacist, can not only follow the progress of the application, but can also keep a history and draw up a well-ordered list. Moreover, once the actual import or export operation is performed, the authorisation can be validated with a single click using NDS-web. In 2015, the system was up to full speed: approximately 95 % of all applications were submitted via this website.



The pathway followed by an application for an import/export authorisation is much quicker when the NDS-web application is used.

Since the entity handles 8 000 import and export authorisations every year, this application offers a considerable administrative simplification for famhp and its partners!

Handbooks and additional information are available on famhp's website*.

Steps towards auto-control

For many years, the Narcotics Team's inspectors have travelled through Belgium validating the import/export of packages of narcotics and of certain psychotropic substances. Every quarter, the precise quantities of these products imported into Belgium or exported to another country must be sent in a timely manner to INCB (International Narcotics Control Board). This organisation is responsible for monitoring the international trade in narcotics and psychotropic substances.

At the end of 2015, a pilot project was launched involving one of our partners: it gave a company responsibility for validating the import/export of packages of narcotics under strict conditions and under the intermittent supervision of inwspectors. In the future, this form of auto control shall be integrated into the relevant legislation. We shall await further developments ...

** www.famhp.be/en/authorisation_import_export*

Materiovigilance and pharmacovigilance combined for famhp's third Vigilance Day

In 2013 and 2014, famhp organised the first two Pharmacovigilance Days, which proved to be very successful. In 2015, famhp cast the spotlight not only on the essential role of famhp in pharmacovigilance, but also on the importance of analysing and monitoring medical devices. This is the reason why the Pharmacovigilance Day was extended to include materiovigilance. A new name was needed to reflect this expansion of the scope, and the logically choice was Vigilance Day.

Another successful event

In 2015 the emphasis was on hospitals. A whole series of related subjects, notably including pharmacovigilance and materiovigilance contact persons in hospitals, were covered from both a pharmacovigilance and a materiovigilance point of view. The event was a success, with more than 200 people attending the 2015 Vigilance Day, most of whom are from the target group. Famhp was particularly pleased to welcome representatives from the pharmaceutical and health products industry, from professional bodies, from the Belgian poison control centre, mutual insurance companies as well as colleagues from the FPS Public Health . Indeed, it is only through meaningful collaboration that everyone can contribute, at his or her own level, towards the improved utilisation of medicines and medical devices and, ultimately, to higher levels of safety for everyone.

From pharmacovigilance to materiovigilance

The opening discussions were on subjects relating to pharmacovigilance, considering the issue of medication errors. Famhp presented its position as a competent authority and described the experience and expertise it has acquired from adopting practical and economic approaches to this issue. During his presentation, former employee Xavier Kurz, who now works for the European Medicines Agency (EMA), explained in detail the detection of signals which has constituted the core aspect of pharmacovigilance since the last recast of the European legislation.

The day also provided an opportunity to meet and exchange ideas and views with the general public via a number of constructive discussions and Q&A sessions.

During the discussions dedicated to materiovigilance, the experts addressed the issue of what is a medical device and the latest developments in the field. This was followed by a presentation of borderline products, which notably demonstrated the difficulty in determining if you are dealing with a medical device, a medicinal product or a combination of both.

The Vigilance Day proved once again to be the ideal opportunity to promote awareness amongst the various target groups of pharmacovigilance and of vigilance with respect to the safety of medical devices.

The increasing importance of medical devices was also emphasised. The natural consequence of this is the particular importance of greater awareness amongst healthcare professionals with regard to the notification of incidents. Although the notification of incidents is a legal obligation in Belgium, famhp considers that one of its roles is to provide healthcare professionals with information about what should prompt a notification and what procedure they should follow.

A greater focus on the surveillance of medical devices

Famhp endeavours to improve the quantity and detail of the information exchanged with the various interested parties, in order to enhance the surveillance of medical devices. The next recast of the European legislative framework shall further contribute to this upgraded surveillance. However, Belgium has acted in anticipation of this European initiative: the Plan for Medical Devices Plan was approved in 2012 and been implemented since that date. One of the main initiatives it has introduced is the central register of traceability, which makes it possible to monitor a medical device from the manufacturer through to the patient. During Vigilance Day 2015, a full description of this traceability register was provided by Vanessa Binamé, who at that time was Director-General of DG POST authorisation of famhp.

The next subject considered was metal-on-metal prostheses and the practical application of materiovigilance in hospitals, with a central role assigned to the materiovigilance contact person.

The Vigilance Day proved once again to be the ideal opportunity to promote awareness amongst the various target groups of pharmacovigilance and of vigilance with respect to the safety of medical devices. The various participants were informed and encouraged to work as a matter of course with famhp to create a safer environment for everyone, especially patients.

In view of the positive feedback received, there is no reason why a fourth event should not be organised.

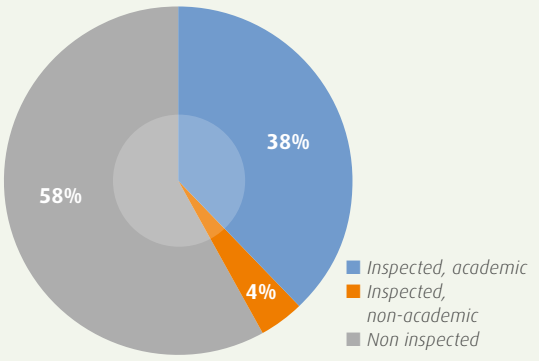
First outcome of the inspection of Good Clinical Practices conducted by the ethics committees

At the start of 2015, famhp's DG INSPECTION launched a programme of inspections of GCP (Good Clinical Practices) to appraise the quality systems implemented by the principal Belgian ethics committees.

The ethics committees authorised to give a single opinion for multi-centre clinical trials, and which are thus fully accredited, were inspected as a priority.

Of the 24 fully-accredited ethics committees, 10 have so far been inspected, including the ethics committees which submit the most opinions each year. In 2016, famhp will ensure that this inspection programme is completed promptly.

ETHICS COMMITTEES



An initial analysis indicates that, although the situation varies greatly from one ethics committee to another, the quality systems implemented must be significantly improved.

Certain issues were identified frequently: consistency of the opinion documentation issued, systems for recording curriculum vitae, declarations of interest, training, at least a yearly revision of the dossiers, etc. It should, however, be noted that no serious deficiency was detected which might compromise patient safety or the ethics of the clinical trials.

This situation is not a direct consequence of any failure on the part of the members of the ethics committees, but is rather due to the other demands placed on their time by their usual work as medical doctors, pharmacists, other healthcare professionals, etc. which often leaves them with very little time to devote to their assessments for the ethics committee. There are also insufficient financial and human resources, which makes it difficult to raise the quality of the structures. Moreover, the aim of these inspections is to make the institutions concerned aware of the situation so that they can invest more heavily in these essential ethics committees which ensure the ethical conduct of clinical trials. Famhp hopes that, ultimately, these institutions will be able to operate in accordance with the legislative framework which they are required to observe.

Despite all the observations made, a real willingness has been noted from all the ethics committees to improve and to work towards compliance with the guidance and legal standards currently in force.

An interview with Ann Adriaensen, the new chair of the Transparency Committee

Mrs Adriaensen, who are the members of the Transparency Committee? What role will this committee play in shaping the future?

All the stakeholders in the Belgian distribution chain (pharmaceutical and medical devices industries, wholesale distributors and (hospital) pharmacists) are represented in the Transparency Committee. Taken together, these sectors provide about 75 % of famhp's revenue. The members of the committee have a very clear picture of what goes on in their respective organisations and consequently they are the ideal persons to guide famhp. I think of the Transparency Committee as a sort of "board of directors", which in addition to overseeing the management of famhp also proposes initiatives which are beneficial for the development and strengthening of famhp. I feel sure that we have the resources necessary to rise to the challenges of the future in a constantly-evolving European environment.

What is the committee's point of view on the future of famhp?

As an innovative country in pharmaceutical terms, Belgium is strategically very important. Many Belgian pharmaceutical companies have a R&D department. This is why famhp is involved right from the first phases in the development of new and often essential medicines. The value of this involvement for the benefit of public health should not be underestimated. Thanks to these clinical trials, patients in Belgium are fortunate in that they gain access to medicinal products in their development phase sooner than elsewhere. This involvement in clinical research also offers numerous opportunities for hospitals, research centres and healthcare professionals. Famhp is the lynchpin, coordinating the work of these various parties. This unique position underlines the importance of famhp for the future: it is the ideal partner for the coordination of new developments, such as early phase development, unmet medical need programmes, as well as in vaccinology. Companies are keen to be involved in building this future with famhp.

New concepts such as Zero Based Budgeting, fee-for-service and activity-based costing are starting to appear. Can you tell us why the committee has assigned such importance to these concepts?

I can understand why many people might feel concerned when they hear zero and budget in the same phrase! However, *Zero-Based Budgeting* is, in fact, a very sensible way to prepare a precise budget, by considering one line item of the budget at a time. This approach prevents any overestimation of costs and makes provision for a margin in the budget which can be used, for example, to fund new projects and for hiring staff. Activity-based costing is a closely linked term and is used to determine the activities for which famhp is responsible and the costs generated by these activities. The costs which famhp incur when providing a service constitute the *fee* which must be considered in comparison with the qualitative service provided. Hence the concept of *fee-for-service*, which simply means paying the right amount for a correctly delivered service; a principle approved by all the stakeholders.
By applying these principles to all famhp's activities, the budget is made completely transparent. The result is an excellent partnership, in my opinion!

You are effectively asking famhp to work in a different way. This represents a great deal of work for famhp employees. As a committee, are you going to help them to accomplish this task?

Absolutely. I am very lucky in that I work with such skilled personnel at famhp. Their contribution will be crucial in seeing this operation through to a successful conclusion. Moreover, this new way of working will not only make famhp more efficient, but will also create numerous opportunities. With staff, management and the Transparency Committee all working together we shall achieve amazing things and shall construct the famhp of the future.

> *"By applying these principles to all famhp's activities, the budget is made completely transparent. The result is an excellent partnership, in my opinion!"*

Famhp invests in financial transparency

Financial processes are closely intertwined with operational processes. This is why, following a recommendation from famhp's financial supervision body, the Belgian Court of Audit, various activities must be recorded directly into the accounting software.

For this reason, the individual responsible for DG INSPECTION's "narcotic drugs order forms" bank account has received additional training and now has total independence when entering banking transactions.

This type of integration provides a further safeguard for banking transactions and guarantees famhp's financial transparency with regard to its partners.

Load shedding, what's that?

Logistics is conscious of the need to set a good example relating to rational consumption of energy and has therefore developed a three-parted eco-plan, in consultation with the Regie der Gebouwen-Régie des Bâtiments (the real estate expert of the Belgian federal state) and the Communication Division. Its aim: to adapt, implement and support energy saving initiatives.

First part: OFF-ON

The Communication Division put in place this plan's first part. Various communications have been generated to address the more wasteful behaviours in terms of energy use. Posters bearing the OFF-ON logo have appeared in kitchen areas, next to photocopiers, etc. Also, an indicator has been included on all LCD screens showing the real-time status of the Belgian electricity grid.

Second part: load shedding

The second part relates to the voluntary reduction in power consumption, otherwise known as load shedding. A memo approved by famhp's Chief Executive Officer lets the agency reduce its consumption, to a lesser or greater extent, as a function of the status of the Belgian supply network. There are four possible levels of reduction, ranging from normal operation (when the indicator is green) through to maximum load shedding (black indicator). Specific measures are associated with each level. These measures guarantee the safety and security of the building and ensure that every employee can return home under good conditions.

Third part: savings over the longer term

The last part relates to a long-term energy saving policy. Each employee has been equipped with a multi-socket standby saver, which fully disconnects PCs and other devices left in standby mode. Motion sensors now switch on and off the lights in kitchen areas and toilets throughout most of the building. Some open-space office areas are also equipped with these devices. A surprising feature: these sophisticated sensors are activated by speech as well as motion! This stops the light from switching off just because no one is moving!

Famhp starts to move towards the New Way of Working

The NWOW (New Way of Working) is becoming increasingly popular in Belgium, as it is everywhere else. Although the movement is not new, it has expanded steadily over the last few years. In a world focused on production, the needs of the individual often take second place behind the need for the results produced. The NWOW movement changes the focus such that the core concern is the satisfaction and fulfilment of the individual. This shift in the focus empowers everyone to participate actively, responsibly and independently, allowing them to succeed in addressing ever more demanding challenges. The introduction of a NWOW requires the implementation of a number of major actions, with changes to the working environment and, particularly, to working practices and management.

Less control, more trust

The principle that our personnel is trustworthy has been the starting point for famhp's new culture, more commonly referred to as the "new way of working" culture. The application of this principle has resulted in modifying employment regulations by not checking the time spent at the workplace anymore. During a subsequent phase, all personnel will be allowed to increase their number of home-working days to the maximum, in compliance with the legislation.

Greater effectiveness leading to more freedom

However, this is no more than a first step, since the most fundamental change is in its practical application, with the changes to working practices. By allowing everyone to work with a focus on achieving their objectives, and on respect for customers, colleagues, and undertakings made on a team level, and by refocusing on what is essential - the agency's mission and the individual's contribution to its achievement - employees feel more independent, more responsible as well as being more creative and productive.

Changing the culture is a long-term endeavour, but the first steps have now been taken. And 2016 will be the year in which NWOW shall be disseminated and adopted.

NWOW

Working with famhp

You would like to help protecting the citizen's health? Working for a federal agency is something that appeals to you? Take part in our recruitment procedures and join our organisation.

The most wanted profiles are:
- doctors, veterinarians and pharmacists with experience, in order to evaluate clinical data for a medicine or health product;
- scientific file managers in order to manage and follow up dossiers regarding medicines and health products;
- administrative collaborators in order to assist the file managers in the quality control of data and documents;
- legal officers;
- computer scientists.

How to apply?

As we are a federal organisation, all our selection procedures are conducted by Selor.

If you wish to apply, you should react to the job ad that will be published on their website (www.selor.be). We strongly advise you to subscribe to their newsletter in order to be sure to receive all the ads matching your profile.

A Service desk dedicated uniquely to application problems

One of the recommendations of the investigation conducted in 2014 by Trasys, a company with expertise in IT, concerned the creation of a level-two Service desk for applications. Concretely, calls arrive at level one, the ICT Helpdesk, where a ticket is created. The tickets are then sent to the teams concerned. From now on, questions regarding an application will be handled by the level-two Service desk. This service is being put in place progressively, based on service-level agreements defining the required quality of service and flow diagrams. The latter describe the path which a ticket takes from reception of the question through to the resolution of the problem.

The first diagrams indicating each step in a process, available as a provisional version and ready for validation, relate to the register of retail pharmacies and the CESP connector (Common European Submission Platform connector). This system makes it possible to connect automatically to the European portal for the submission of marketing authorisation files or of registration files for medicines.

The aim in the medium term is to introduce process diagrams for each application used by famhp, in order to offer a better service to users.

More workspace for famhp

Famhp shares the Eurostation building with a number of other organisations, such as the FPS Health, Food Chain Safety and Environment, and the World Health Organisation. To accommodate the agency's constant development and growth, The Colleagues of Logistics have held various discussions with their neighbouring organisations and with the Regie der Gebouwen-Régie des Bâtiments (the real estate expert of the Belgian federal state) to increase the amount of space allocated to famhp. The outcome is that an additional secure zone has been made available which now accommodates a canteen for famhp personnel and four conference rooms dedicated to internal meetings.

The soft control policy

To ensure the quality of the services provided by Logistics, at the start of the year a new team was tasked with checking the services delivered.

For the first phase of this initiative, Logistics identified nine key tasks:

1. building management;
2. management of equipment and of the purchasing department;
3. logistic support;
4. catering;
5. reception;
6. mailroom;
7. archiving of documents;
8. organisation of events;
9. cleaning.

The next step was more difficult. It involved determining the points which require attention and to which a soft control policy could be applied, with the purpose being to check the activities in an effective and inexpensive manner.

Visible improvements

Whenever a request for an improvement or a complaint is received, the subject is discussed within the Logistics Network, which brings together all famhp entities, and by the staff of Logistics. It is certainly in this respect that the greatest change has been made, since from now on, the priority is to enable everyone to observe for him/herself the progress which he/she wanted to be made. Whilst this policy requires a certain creativity and a good dose of imagination, it also significantly increases satisfaction levels in our team and amongst famhp employees. For example, wall-mounted posters in washrooms allow everyone to check that the daily cleaning tasks have been performed. Another example is the availability of coloured chairs in meeting rooms.

Guaranteed execution of checks

Unfortunately, it is not always possible to apply soft control. In this case, Logistics passes on the verification task to our back-office team, which takes responsibility for dealing with all the requests and ensures that the equipment is working correctly. An example of this type of verification is the monthly check of the use of the meeting rooms or the weekly check of the equipment used in these rooms.

Positive impact on the budget

This soft control policy also has an effect on budgetary aspects. Accounting now maintains a table for monitoring the expenses accrued by the various inspectors. This active monitoring of expenses claims forms is used to detect and send out reminders for overlooked declarations. This system should ensure that famhp can make provision for the amounts owing for these reimbursements and, ultimately, to provide timely reimbursement for payments made.

Telephony migration at famhp

In order to modernise its communication systems, famhp has taken back the management of its telephony, previously provided by the FPS Public Health.

Phase I: changing the telephone numbers

The first phase started in spring 2015 and was completed at the start of the autumn 2015. Its aim: to change all our telephone numbers.

In order to have the least possible disruption, both for famhp personnel and for our partners, we simply transferred over the existing functionalities.

Working closely with the Communication Division, which made sure that our various partners were given the new numbers, the IT teams switched-over all the telephone numbers on 1 October 2015. Mission accomplished without incident!

Phase II: modernising the communication systems

November 2015 marked the start of the second phase of the migration.

To satisfy the requirements associated with the future move to Boulevard Pacheco and to offer the greater flexibility demanded by the NWOW (New Way of Working) culture, the current landline system will be completed by softphones.

The test phase began on a limited number of users. The process will continue in 2016 with a broader set of test users, and will culminate in the entry into service of softphones within the agency.

What benefits are to be gained from modernising our communication systems? Increased flexibility for personnel, greater availability to serve our partners better and improved responsiveness to their needs.

Zero Based Budgeting, a new perspective on our financing

Famhp is a federal parastatal organisation. This status places it in a fairly rigid framework with regard to obtaining authorisation for its expenditure. Indeed, every year, the budget-setting authorities determine the ceiling for the rate of growth or the savings which have to be made for the following year. This approach only slightly considers the specific financial context for our agency: the preponderance of internal financing.

Up until now, the agency has been able to count on support from partners represented on the Transparency Committee. Famhp has thus been able to operate beyond the traditional guidelines and thus fund new activities. Numerous projects have been started or indeed strengthened: the Medical Devices Plan, the strengthening of AUDIT JAP, the enhancement of expertise, the new European pharmacovigilance obligations, the renewal of the Commission for medicines for human use etc.

Investing in improvement projects

Private-sector partners (which provide financial support) are now asking famhp to investigate whether or not improvement projects can be initiated while keeping their contributions at the same level. Note that the objective being pursued is not to make savings, since the financial resources will continue to be allocated to famhp. The resources ultimately granted will be invested in improvement projects. And if analysis shows that the resources needed to fulfil the mission must be increased, then they will be increased.

Famhp has thus launched an analysis based on the Zero Based Budgeting methodology. The aims targeted by this methodology are to obtain:

- greater transparency and better estimation of the cost of the agency's outputs,
- alignment between famhp's revenue and the financing of its outputs: WHO pays for WHAT and HOW, and in a fee-for-service context,
- an analysis of the outputs with a view to producing a budget which reflects the actual requirements. This means that a balance must be reached between efficiency and quality of the outputs in a public health context.

The ZBB mission started in February 2015 and will continue over the coming months.

A new structure for the Homeopathic & Herbal Medicines Entity

In 2015, the Homeopathic & Herbal Medicines Entity was significantly restructured and is now part of the Marketing Authorisation (Human) Division of DG PRE authorisation.

The main projects in 2015 in relation to homeopathic medicines

The ultimate objective of this entity with regard to homeopathic medicines is the timely handling of applications for registration and MA (Marketing Authorisation) for homeopathic medicines. To achieve this aim, the agency completed a number of improvement projects in 2015.

In consultation with the pharmaceutical industry concerned, the database of notified homeopathic medicines has been revised since 2014. This new list which, in 2003, contained 18,000 notified homeopathic medicines has now been slimmed down to just 5,654. An application has been developed to manage changes to the notifications for the products in this new list. This application can also be used to provide rapid and accurate answers to questions, both internal and external, about notifications.

The Homeo version of the electronic dossier management system (MeSeA: Medicines e Submission and e-Approval) was rolled-out at the end of 2014 and quickly reached full operational status during 2015.

Over the course of 2015, discussions were held between the sector and famhp to review the funding of the entity's activities. The outcome of these discussions was a consensus: firstly, the fees charged for dossiers are adapted and, secondly, the operators in the pharmaceutical industry concerned should contribute to the funding, with the value of their contribution based on their sales turnover.

A discussion was also initiated regarding the operational effectiveness of and the collaboration with the Commission for homeopathic medicines for human and veterinary use. This discussion led to the creation of a SLA (Service Level Agreement) which specifies the procedure which must be followed for the various types of dossier. This SLA was adopted by the aforementioned commission in July 2015.

Finally, during fresh discussions with the homeopathic sector at the end of the year, famhp formulated a number of proposals regarding the operation of the entity in 2016. The aim of these proposals is to strengthen the interaction between the homeopathic sector and famhp and to define the priorities for the management of dossiers.

Herbal medicines

To enable it to handle the various types of herbal medicine dossiers, the entity was keen to meet with the various services concerned. This transverse consultation resulted in concrete agreements to define optimally the handling of the various stages of the dossier, from validation and assessment through to closing.

Joint audit of notified bodies: from voluntary to mandatory

Following the joint audits conducted on a voluntary basis in 2013 and 2014, the mandatory joint audit system has now been introduced! This system came into operation in 2015 and applies this time to all notified bodies which issue the CE marking of medical devices. In Belgium, two notified bodies have already been audited under this new system and our inspectors have taken part in two other audits outside Belgium.

Summary of the voluntary system

Between January 2013 and November 2014, 25 inspections of notified bodies were performed in 23 countries of the European Union in the context of a joint voluntary action. The aim was to assist the national competent authorities in their supervision of notified bodies. Each team of national auditors was accompanied by experts from the FVO (Food and Veterinary Office) and by auditors from outside the host country. Famhp performed 7 missions, involving 3 inspectors, in Belgium and in other Member States.

The final assessment: valuable

At the end of this joint voluntary phase, the process was assessed as positive for both host countries and the external experts. Everyone had the opportunity to exchange ideas and points of view with their colleagues. There were no major disagreements between the teams led by the European Commission and the national authorities. In a few rare cases, the scheduling and detail of the audits were debatable but the degree of expertise necessary for the supervision of the notified bodies was always judged to be acceptable.

Overall performance of the notified bodies

From a general point of view, the joint voluntary audit system succeeded in establishing within the European Union a standard performance level* necessary for the inspection of notified bodies. This system also proved to be valuable in obtaining an overview of the performance of the national authorities in the field. However, a number of notified bodies were not able to provide sufficient evidence to establish the qualification of the personnel they use to carry out certification activities. Other recurrent problems notably involved the degree of detail of the review of clinical data, the samples selected from technical dossiers and the documentation for the certification process. In all these cases, the notified bodies were obliged to put in place measures to correct the problems encountered. Sanctions and restrictions, varying in severity up to "de-designation", were imposed in the severest cases of nonconformity.

From a general point of view, the joint voluntary audit system succeeded in establishing within the European Union a standard performance level* necessary for the inspection of notified bodies.

* *Implementing Regulation (EU) No. 920/2013*

MS Project Server and proof of concept

With a view to improving the planning and monitoring of projects, the ICT Division decided to install MS Project Server. To validate the feasibility of this project and to specify its configuration, a proof of concept (POC) environment was set up.

Based on this POC, the decision was taken to create the following functionalities:
- project management,
- planning,
- team working,
- project reporting,
- resource management,
- task management,
- problem management,
- timesheets,
- risk management.

Based on the experience acquired, the production environment will be set up in 2016.

DG INSPECTION adapts its inspection policy

To keep pace with the increasing complexity and number of products, fields and sectors inspected by famhp, work has begun on adapting the inspection methodology in the context of a priority project initiated by the Belgian minister for Public Health, Maggie De Block.

The project, its objective, its goals

DG INSPECTION is looking to adapt its current inspection policy by implementing a new methodology designed to:
- promote synergy and co-regulation between inspected enterprises and famhp;
- promote transparency and administrative simplification;
- optimise the efficiency of the controls.

Auto control as the first step

This project is estimated to last three years. During phase one, scheduled to run from 2015 to 2017, the aim is to put in place a auto control system in the field of medical devices. In conjunction with this system, the inspection services shall conduct risk analyses to rationalise the planning and execution of the inspections performed in the field.

During this initial phase, famhp plans to make it a legal requirement for Belgian operators in the medical devices sector to register their activity so that they are known to its services. The operators on this register will have to provide DG INSPECTION with the data it needs to conduct risk analyses. There are also plans to offer service users the option to follow the applicable recommendations so that they can carry out auto control. These recommendations shall be drafted by the inspection services in conjunction with the professional organisations in the medical devices sector.

The operators concerned shall be responsible for the conformity of the information passed on and for regularly updating this information. They should also provide confirmation to the inspection services that they comply with the recommendations provided.

To facilitate the exchange of information, famhp inspectors use an IT portal, set up specifically for auto control, as the exchange interface between operators in the medical devices sector and famhp.

A project team consisting of personnel from the ICT and Legal Affairs Divisions and from DG INSPECTION has now been created within the agency to bring this first phase of the project to completion. In view of the extent of this first phase, DG INSPECTION plans to start up auto control at the end of 2016 within one segment of the medical devices field: notified Belgian distributors. The implementation of auto control in the field of medical devices should be finalised in 2017.

Sharing responsibilities with the medicinal products sector

The aim is to pursue the project during a second phase, from 2017 to 2018, working towards co-accountability and co-regulation between famhp and the medicinal products sector. The exchange interface developed during phase I to promote administrative simplification, could then be used to optimise the efficiency of the planned and performed inspections.

Between now and the end of 2016, the approach with regard to the pharmaceutical sector and blood transfusion institutions shall be defined jointly with the associations of representatives of these sectors.

And finally, after implementing and assessing phases I and II, famhp shall consider regulating the delegation of inspection work via a partnership with the sector or, depending on how the project develops, via an independent organisation. Naturally, famhp shall retain the right to conduct targeted inspection actions on the premises of the operators concerned and of the organisations to which inspection work has been delegated.

There are also plans to offer service users the option to follow the applicable recommendations so that they can carry out auto control.

Unmet medical need: the new legislation is implemented

Some patients suffering from severe or chronic diseases cannot be treated satisfactorily with the medicines currently available on the market. This is known as an UMN (Unmet Medical Need).

In order to speed up access to innovative medicines, famhp established in 2014 a new procedure which temporarily authorises the putting in place of a so-called Compassionate Use programmes, or Medical Need programmes, and thus treats the patients concerned.

2015: sessions on dissemination of information, implementation, evaluation etc.

In 2015 the focus was on the dissemination of information about, and the implementation of the new legislation on UMN. Accordingly, famhp organised an information dissemination session for its external partners with the aim being, on the one hand, to present the various legislative aspects and, on the other hand, to listen to the problems encountered by companies with the implementation of this legislation. Subsequently, another event was held at BRAS (Belgian Regulatory Affairs Society) during which we presented an assessment almost one year after the entry into force of the new Royal Decree.

In addition to communications to pharmaceutical companies, an information dissemination session has also been organised for the ethics committees involved in the process of evaluating UMN dossiers.

And adaptation

Following on from these initial events, we organised working groups set up to consider various subjects in order to clarify certain aspects of the legislation and to adapt accordingly the documents available on famhp's website. These documents are, moreover, the product of collaboration with representatives from the General Association of the Pharmaceutical Industry (pharma.be).

At the same time, the UMN team has drawn up the standard operating procedure within famhp to harmonise the handling of the dossiers and ultimately to improve the quality of the handling of the latter.

New partnership with RIZIV-INAMI

In cases where the temporary use of a medicine is authorised, famhp also provides, jointly with RIZIV-INAMI (National institute for sickness and disability insurance), the secretariat of the CATT-CAIT (Advisory commission in cases of temporary intervention) on which representatives from the agency have a permanent seat.

2016: a renewed commission for medicines for human use

The process will be optimised in 2016 with the setting up of the renewed commission for medicines for human use, which will play a key role in the implementation of the new legislation.

A new-look for the Commission for medicines for human use

What is CGH-CMH?

CGH-CMH is the Commission for medicines for human use. Its role is to provide opinions on marketing authorisations; on making medicines available to patients in the context of so-called CUPs (Compassionate Use Programs) or MNPs (Medical Need Programs); on pharmacovigilance and on scientific questions regarding medicines. This commission is in the process of being revamped (composition, operation and competences) within famhp.

Keeping pace with the current reality

In 2015, the legislative framework for the Commission for medicines for human use was revised. The changes focused particularly on an adaptation to the Royal decree of 14 December 2006 on medicinal products for human and veterinary use. The aim is to maintain the commission's ability to handle the ever more extensive range of medicines, e.g. in terms of Advanced-Therapy Medicinal Products (ATMP), on which CGH-CMH must also deliver opinions. For this reason, the areas of expertise provided by the members have been adapted so as to create the broadest possible scientific and clinical coverage. CGH-CMH now comprises eight full members and eight substitute members with experience and knowledge in the following areas of expertise: general healthcare, general medicine, paediatrics, pharmacology, advanced therapies, hospital pharmacy, internal medicine and genomics/personalised medicines.

A carefully selected revised commission

For each area of expertise, one full member and one substitute member were appointed as the culmination of a process which involved contacting every Belgian academic centre and academic hospital. Famhp received a great many positive responses and applications. Each candidate was then invited to attend an interview so that his or her motivation and vision for the Commission for medicines for human use could be assessed. Once the proposed composition of the commission had been validated by the strategic cell of the minister for Public Health, Maggie De Block, famhp was able to publish, in the Belgian official journal, a ministerial decree which gave formal notification of the new composition of this renewed commission.

In-depth restructuring

To ensure optimal operation, several important changes have been adopted:

- the existing procedures have been reviewed and specified in more detail;
- the CGH-CMH shall sit every week, instead of once a month which is the current frequency;
- significant changes to the commission's internal regulations have also been prepared.

The agency hopes that this restructuring will improve the quality and quantity of the scientific opinions it provides and broaden their scope to cover the entire lifecycle of medicines. Moreover, subjects not directly linked to a dossier could be submitted to the commission, such as the revision of orientation documents (guidelines). This restructured commission should ensure that famhp can optimise its decision-making process, both for national and European dossiers, to strengthen further its position within the European network.

The patient remains our core concern

Since listening to the patients' points of view is crucial for our agency, this group clearly deserves representation within the CGH-CMH via organisations which represent patients. The appointment of the patient representatives is scheduled for 2016. Finally, famhp shall , in cooperation with the strategic cell, also implement the necessary measures to ensure representation of the ethics committees.

Greater visibility for Risk Minimisation Activities

For some medicines, RMAs (Risk Minimisation Activities) are required to ensure use that is as safe as possible. The granting of marketing authorisation for these medicines is conditional on the implementation of these RMAs.

RMAs are added to the recommendations indicated in the summary of product characteristics and in the patient information leaflet, which are mandatory for all medicines. These additional RMA have been conceived for three reasons:

- to minimise the adverse reactions and risks associated with certain medicines;
- to ensure correct administration and safe and effective use;
- to prevent the risk of a medical error.

These RMAs may, for example, involve providing educational material intended to give prescribers appropriate information about a medicine whose administration may present particular risks, to allow them to determine whether or not the patient is eligible for the treatment, to monitor the risks during the treatment and to manage optimally the adverse reactions identified. Examples are brochures, checklists, therapeutical indication/dosage information cards, instructions for administration/use, dosage calculation rules and training.
Educational material may also be developed for the attention of patients to promote the proper use of the medicines. Examples are brochures, cards, treatment and consent forms, guides and DVDs.

Improved access to RMAs

The various educational materials are available on famhp's website.
Moreover, the pages relating to these materials have been restructured so that BCFI-CBIP (Belgian centre for pharmacotherapeutic information, non-profit association) can create a link, on its own website, between each medicine concerned by RMAs and the specific material(s) developed by the marketing authorisation holder for the medicine and which have been approved by famhp. The medicines concerned can be identified on BCFI-CBIP's website using the ▼ symbol (downward-pointing orange triangle). A click on this symbol takes you to famhp's website, from which RMA documents for the medicines concerned may be downloaded.

BCFI-CBIP website: www.bcfi.be – www.cbip.be

SharePoint: who, what, how?

What?
SharePoint is an electronic document management and sharing tool which facilitates collaboration between famhp's various collaborators.

How?
The use of standard documents speeds up the process of making collaborative websites available to users. In 2015, more than 130 document-sharing websites were created in this way.

Examples include:

- for the management of meetings: agendas, invitations and associated documents including their history;
- for project management: ideas and assessments of projects, and progress status reports;
- for the Legal Affairs Division: legislative dossiers, the management of litigations and requests for new legislation.

Who?
SharePoint officers for the agency's various entities have been trained in the creation and management of new websites. For every new website, the SharePoint officer for the entity concerned must submit a request form to the ICT Division.

Famhp has also started to use workflows to validate the documents. And a procedure has also been put in place by the SharePoint team for the archiving of websites which are no longer live.

(T)ACs up and running

The concept of (T)ACs ((Therapeutic) Area Coordinators) has been established. Why? On the one hand to monitor medicines effectively throughout their development and life cycle and, on the other hand, to perpetuate the clinical expertise needed within famhp. These objectives also help to support the renewed Commission for medicines for human use.

How does it work?

Concretely, for each therapeutic area, a therapeutic area coordinator is appointed within the DG PRE authorisation's team of clinical evaluators. He/she is assisted by one or more experts in the area and by their back-ups. How can all the relevant areas be covered and how can the continuity of the monitoring be ensured? Each TAC may also be an expert in an area other than his/her own area.

Area coordinators have also been appointed in areas whose scope is more horizontal, such as pharmacokinetics, biostatistics or advanced therapies. And a grid has been established to specify the responsibilities of the various clinical evaluators in each therapeutic and horizontal area.

What is the role of (T)ACs?

TACs must perform risk-benefit analyses throughout the development and life cycle of the medicines, including during the evaluation of the various applications submitted in relation to this medicine (clinical trials, scientific advice, MA (Marketing Authorisation), medical need programme, etc.). Naturally, this analysis is the product of consultation with the other evaluators engaged in examining the application (pharmacokinetics, non-clinical, quality, vigilance, etc.). TACs also monitor the scientific literature, directives and key changes and ensure that the decisions made in their area are consistent. They are also involved in the identification of unmet medical needs.

When an application is submitted, the clinical data may be evaluated by TACs, but also by experts in the area or back-ups.

Finally, TACs also play an important role in the development of a network of external experts who can give advice about the tasks mentioned previously.

The role of ACs is similar in horizontal areas, with the difference being that they do not assume responsibility for benefit/risk-analysis nor for the identification of unmet medical needs, although their input may prove to be useful.

A system developed one step at a time

The therapeutic and horizontal areas were attributed during an initial allocation within the clinical team in 2013. Given that, at that time, the team consisted of numerous new evaluators and that it has been further strengthened subsequently, it has been necessary on several occasions to refine and reallocate certain responsibilities.
Thereafter, in 2014, famhp was ready to examine in more detail the role of TACs in a series of key areas, via a pilot project. TACs concerned thus drew up a plan for allocating tasks and specified the main requirements necessary to secure the durability of their area. In this way, famhp was able to identify the need for better circulation of information about clinical trials (DG PRE authorisation, R&D Division (human)) and better collaboration with the pharmacovigilance evaluators (DG POST authorisation).

Based on the experience acquired during the pilot project, famhp experts generalised the system of TACs during 2015. The interaction with R&D Division (human) in the context of clinical trials was reinforced through better circulation of information about on-going trials and better collaboration during benefit/risk analysis of clinical trial applications. Moreover, collaboration between TACs and pharmacovigilance evaluators has also been strengthened.

Assessment and improvement

In 2015, a semi-quantitative KPI (key performance indicator) was developed in order to be able to monitor the level of durability of the various areas. This KPI considers internal expertise (including the development status of the tasks conducted by TACs or ACs, the number of experts in the area and the number of back-ups) and the network of external experts. In the middle of the year, the results of this KPI revealed that the durability was insufficient in a certain number of areas (namely the areas in which there are high numbers of new applications or marketed products and/or those which hold specific interest for famhp). The agency has, of course, considered these results when setting the objectives for the clinical evaluators. At the end of 2015, this strategy resulted in much better durability of the targeted areas, according to the pre-established KPI.

Projects for 2016 ...

Due to the optimisation measures taken in 2015, the development of the TAC system has been such that it can adequately support the new-look Commission for medicines for human use, as from the start of 2016.

The system should clearly once again be further developed and rise to new challenges:

- the depth of the expertise may be increased and the various therapeutic and horizontal areas further refined;
- collaboration with patient organisations will represent a challenge for TACs;
- depending on the early access to medicines initiatives, the link with evaluators from RIZIV-INAMI (National institute for sickness and disability insurance) will be used even more;
- the semi-quantitative KPI will continue to be used to monitor regularly the durability of the expertise, in order to make adaptation possible.

TACs must perform risk-benefit analyses throughout the development and life cycle of the medicines, including during the evaluation of the various applications submitted in relation to this medicine (clinical trials, scientific advice, MA (Marketing Authorisation), medical need programme, etc.).

Some results obtained using the TAC system

- For the centralised procedure for obtaining an MA, the agency can put forward teams of competent evaluators when it is a candidate to be a rapporteur. In this way, famhp improves its chances of obtaining the dossier. And by making these teams available once it has been awarded the dossier, the experts improve the quality of the evaluation. Up until now, the agency has particularly focused on the vaccines, oncology and diabetes areas, although famhp has also been designated as rapporteur in other areas.
- The internal evaluators are increasingly able to collaborate in terms of requests for scientific advice, both on a European and national level. This is an important factor in view of the moves towards early access to medicines.
- The network of external experts has grown, both in terms of the number of experts and new areas.
- The team of clinical evaluators is better able to provide a rapid and high quality response to questions from other public institutions, from the political world and from the media.
- Collaboration with other public institutions has been strengthened, including with regard to personalised medicines, vaccines, antibiotic resistance and UMN (Unmet Medical Needs).

The AMR action plan: accomplishments in 2015

In 2015, the Medicines for Veterinary Use Division was once again required to allocate significant resources to addressing the issue of resistance to antibiotics, also referred to as Antimicrobial Resistance (AMR).

There is no doubt that the widespread use of these medicines is one of the principal factors promoting the natural selection and spread of antibiotic-resistant bacteria. Limiting their use and avoiding prophylactic administration wherever possible should help to preserve the efficacy of these medicines. For this reason, the prevention of disease and biosafety measures are a priority concern on all farms.

A tax on antibiotics

Since 1 June 2014, a tax has been levied on the packaging of antibiotic products marketed in Belgium and is paid by the MA holder. It is charged both on medicines intended for food-producing animals and on those intended for pets. This tax is higher for medicines which contain critically-important antibiotics, such as third or fourth generation cephalosporins, fluoroquinolones or macrolides. The revenue collected is used to finance the various actions performed as part of famhp's AMR action plan.

Recording the quantity of antibiotics sold

The quantity of antibiotics intended for veterinary use and sold in Belgium is reported yearly based on the data collected by the BelVet-Sac enquiry (Belgian Veterinary Surveillance of Antibiotic Consumption). The data are provided by wholesalers-distributors and manufacturers of medicated animal feeds. The figures revealed a 12.7 % reduction in the consumption of antibiotics between 2011 and 2013. This downward trend did not, however, continue in 2014 (+ 1.1 %). The agricultural sectors are, nonetheless, keen to honour their commitment to a 50 % reduction in consumption by 2020. Sales figures are also analysed on a European scale, wherein Belgium is considered as a major user (it ranked seventh out of 26 member states in 2013, and fifth according to a report from ESVAC (European Surveillance of Veterinary Antimicrobial Consumption)). Note that this classification is based on an analysis of different farming systems across Europe.

Development of a data collection system for determining quantities on a farm level

In order to promote a sense of individual responsibility among farmers and veterinarians, the Sanitel-Med data collection system will be rolled out over the course of 2016. The quantity of antibiotics supplied or administered by the veterinarian shall be recorded for each farm and for each species of animal. This will provide the veterinarian and farmer with a clearer picture of the farm's consumption compared with that achieved by other farmers. Over the coming years, famhp will be vigilant in checking that veterinarians comply with the legal requirements in terms of the quantities recorded and how the antibiotics are used. The purpose of this system is also to promote the implementation of the additional biosafety measures needed on each farm.

Financial support to the non-profit association AMCRA

Famhp provides 30 % of the funding for the non-profit association AMCRA (the centre for antibiotic use and resistance for animals in Belgium), which conducts essential awareness-raising work within all the sectors concerned, with a view to promoting the responsible use of medicines, via the publication of guides to the correct use of antibiotics, awareness campaigns, proposals for self-regulation measures, etc.

Putting in place a regulatory framework

Famhp has worked with the other public services concerned (FASFC and FPS Health, Food Chain Safety and Environment) on a draft royal decree concerned with providing support for the AMR action plan. Indeed, the requirement to record antibiotic-related data in the Sanitel-Med system must be made legally binding. A proposal has already been put forward to limit the use of critical medicinal products in veterinary medicine, based on a prior diagnosis and an identification of the intolerances.

The prevention of disease and biosafety measures are a priority concern on all farms.

Improved management of the register of exited medicines from medicinal stocks at veterinarians

A medicinal stock at veterinarians is a place in which all the medicines that a veterinarian may have to use to treat animals are stored. Each stock is managed by a depositary veterinarian.

The depositary veterinarian is responsible for ensuring compliance with the obligations under the legislation relating to the supply and the content of the medicinal stock and, where appropriate, to the medicines he/she administers or supplies. Famhp gives an identification number to each medicinal stock.

In order to provide traceability of the flow of medicines used in his/her medicinal stock, the depositary veterinarian must keep a register in which he/she records each supply or administration of medicines; this is the register of exited medicines.*

Famhp inspectors started inspecting medicinal stock at veterinarians between 2007 and 2008. Once harmonised, the inspections revealed that the most common infringements related to the register of exited medicines. In 2010, the first data collected revealed that 8.7 % of the inspections found no such register, and 43 % of the inspections found that the register did not conform.

These figures fell by 25 % in 2011 and 2012, following an itinerant campaign conducted by veterinary inspectors in each province of Belgium. These inspectors then carried out actions/inspections on this specific subject in 2014 which resulted in the figures being halved compared with 2010 (4.7 % and 24 % respectively).

Feedback from the veterinary inspectors in the field prompted famhp to continue the action on this specific subject in 2015. And the good news is that the figures indicate further improvements in how well veterinarians are keeping the register of exited medicines. However, this register of exited medicines will continue to be a focus of particular attention, since it forms the cornerstone of the traceability system for medicines used in medicinal stock at veterinarians.

** Article 3, § 2 of the Royal decree of 23 May 2000 on particular provisions regarding the holding of a depot, the purchasing, prescription, supply and administration of medicines for veterinary use by the veterinarian and regarding the holding and administration of medicines for veterinary use by the individual responsible for the animals.*

Good news: legislation purely for medicines for veterinary use

The draft regulation of the European Parliament and of the Council of the European Union on medicines for veterinary use was published by the European Commission in September 2014.

Its aim: to replace the current directive on medicines for veterinary use (Directive 2001/82/EC amended by Directive 2004/28/EC) and elements of another European legislative text relating to the authorisation of medicines for veterinary use (Regulation (EC) No 726/2004). This draft relates to the manufacturing, marketing, import & export, distribution, sale, pharmacovigilance, control and use of medicines for veterinary use.

The aims of the new proposal are:

- to reduce the regulatory and administrative burden;
- to stimulate innovation and competitiveness;
- to promote the internal market;
- to make medicines for veterinary use more widely available, particularly for the so-called "minor species";
- to tackle the risk associated with antibiotic resistance on public health.

This draft regulation will remove the link between legislation for medicines for veterinary use and that for medicines for human use. This legislation will meet the specific requirements of the veterinary sector, by considering its structure.

Discussions, consultations and negotiations

In 2015, famhp organised a consultation process with its various partners, with other affected organisations and with political bodies. These exchanges clarified not only the draft regulation in general, but also the important provisions for the concerned parties. Constructive discussions were held to consider the advantages and disadvantages of the proposal, potential missed opportunities and the impact on the sector.

Before the new regulation comes into force, the member states must agree on a definitive text. These negotiations are progressing within the working group of the Council of the European Union, in Brussels. In 2015, during the Italian and Luxembourgish presidencies of the Council, the working group met 11 times with representatives from the 28 European member states and of the European Commission. This corresponds to the first reading, in accordance with OLP (Ordinary Legislative Procedure), during which the technical content of the entire proposal was examined. Within famhp, the Medicines for Veterinary Use Division, the Vigilance (pharmaco, materio, haemo, bio) Division, the colleagues of DG INSPECTION, which handle the dossiers relating to medicines for veterinary use, and the International Relations Unit were closely involved in the preparation of the Belgian positions. In each working group, famhp was represented by one or more experts, in some cases assisted by the permanent Belgian representative for public health.

Following on from this first reading, the initial proposal of new regulations shall now be reworded by the presidency of the Council (in 2016, it is the turn of the Netherlands and Slovakia) supported by the European Commission and the Council Secretariat. Fresh negotiations with the 28 member States could then begin. The member states' negotiating mandate shall begin as soon as consensus is reached on a reworked proposal. At this stage, the European Parliament shall also participate in the negotiations and the trilogue shall thus be formed.

In parallel to the work of the Council working groups, the draft regulation project was examined by the European Parliament. In 2015, the Committee on Environment (ENVI) and the Committee on Agriculture (AGRI) proposed a series of amendments as consultative committees. The European Parliament shall vote on the draft at the start of 2006 and this document shall then be used as input material for the trilogue between the Council, the Parliament and the Commission.

A long process

Legislative negotiations generally last for 2 to 3 years (between 20 and 35 months). Indeed, the last revision of the directive (Directive 2004/28/EC) took 26 months. The final version of the regulation on medicines for veterinary use could reasonably be expected to be approved by mid-2017. Based on the current adoption period, the new regulation could thus enter force in mid-2019, since the regulation can only enter force throughout the member states 24 months after its publication in the Official Journal of the European Union.

This draft regulation will remove the link between legislation for medicines for veterinary use and that for medicines for human use.

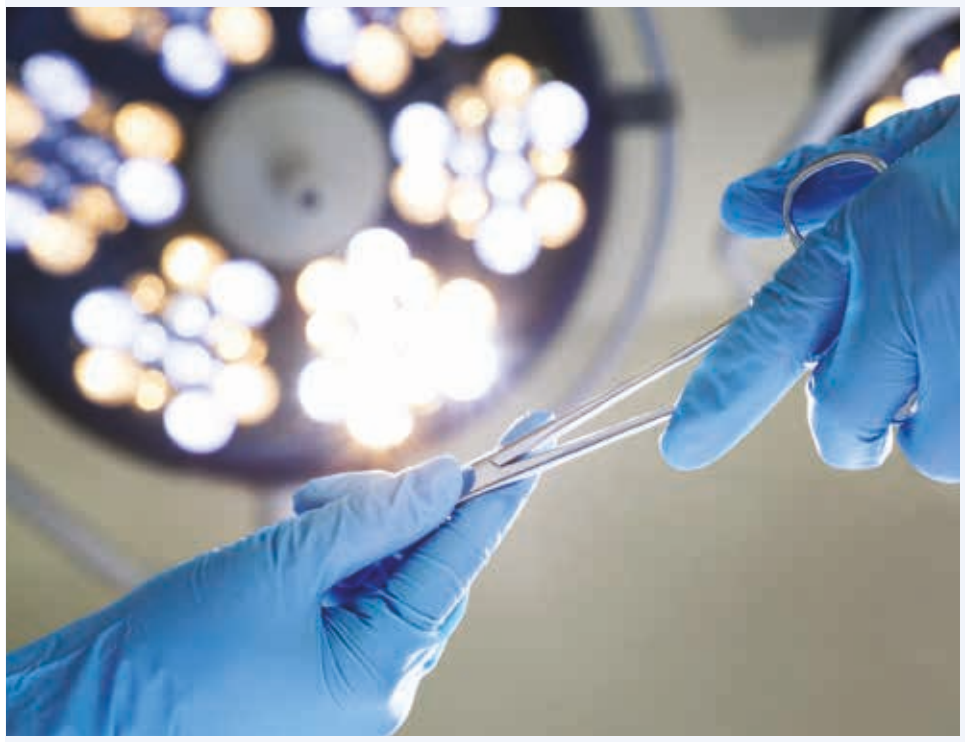
New developments for clinical trials

In 2015, famhp helped to implement the Clinical Trials Regulation, which was published on 27 May 2014.

In the European Union ...
A great deal of work has been carried out to design and develop a European portal for the submission and processing of clinical trial applications, using an entirely electronical process. Famhp personnel participated in the various working groups tasked with defining the criteria applicable to this portal. And in October 2015, EMA (European Medicines Agency) circulated the programme for this new system: since the Clinical Trials Regulation shall not enter into force until a period of six months has passed after the portal is considered to be operational, the date for the entry into force of the Clinical Trials Regulation has been provisionally set for October 2018. More detailed information regarding the exact date and the procedures are expected in 2016.

And closer to home?
With regard to Belgium, the focus in 2015 was on defining the model for collaborative working between the ethics committees and famhp, at the initiative of the minister's strategic cell. Various collaboration options were examined in detail, also considering both legal and budgetary factors. In 2016, famhp thus hopes to be able to announce concrete changes to all the individuals concerned.

New scope of competence for famhp: the inspection of medical devices in hospitals



In the aftermath of the PIP (Poly Implant Prothèse) breast implant scandal, in 2010 the Belgian government approved a new project aimed at improving public health in relation to medical devices: the Medical Devices Plan or PMH-PDM.

Its aims are to improve the traceability of implantable medical devices, and to improve the evaluation and inspection of medical devices in general. This plan has a clear purpose: to increase the quality, safety and efficacy of medical devices and to withdraw any devices that do not meet the minimal European requirements.

A broader scope of competence for the agency

In the context of PMH-PDM, famhp's competence has been extended; this has made it possible for the agency to increase its pool of inspectors dedicated to the inspection of medical devices as well as to widen the scope of the inspections. This gave famhp everything it required to tighten up the inspections performed wherever medical devices are manufactured, distributed or dispensed.

In the past, the Dispensing Division's inspections within hospitals were performed via the hospital pharmacy and primarily considered medicines. In November 2014, the decision was taken to conduct, alongside the existing inspections, inspections specifically concerned with medical devices. The number of contact persons within each hospital increased; however, it was noted that some of them were not even aware that they were responsible for medical devices. To respond to this situation, the Dispensing Division drew up a specific methodology in order to inform these new contact persons of the existence of famhp and of its mission.

Inspection of medical devices whose distribution is not regulated

In addition to medicines, the hospital pharmacist is also responsible for medical devices. These are primarily sterile implantable medical devices, whose distribution circuit is regulated. These devices must be taken up, stored and dispensed by the pharmacist. The hospital pharmacist is not responsible in any way for the other classes of medical devices.

Famhp's new competence, awarded in August 2013, broadens the scope of its investigations to cover classes of medical devices whose distribution is not regulated. For these, the hospital pharmacist is not required to perform take-up, storage or dispensing. Neither is he/she responsible for their quality. The medical devices primarily concerned are:

- measuring equipment;
- traction equipment;
- hospital beds, wheelchairs, stethoscopes;
- invasive devices used in surgery ...

To identify the new contact persons concerned by these new inspections, the agency first had to determine which hospital departments were responsible for the acquisition and maintenance of medical devices, e.g. Purchasing, Logistics, Public procurement, Biomedicals ...

First contact with the new contact persons

PMH-PDM comprises various actions, particularly relating to materiovigilance. The Dispensing Division decided to be guided by these actions when making contact with the new contact persons in each hospital, notably via a targeted action on hospital beds.

Famhp asked DG POST authorisation's Materiovigilance Entity to provide all the notifications relating to hospital beds. It was apparent that very few notifications were issued by hospitals in relation to hospital beds. During the agency's inspections, the various incident scenarios appeared to always lead to the same conclusion: if the incident is handled within the hospital, and even though the information is occasionally passed on to the manufacturer, with a few exceptions (e.g. involving a death), no notification of an incident involving a bed has been reported to famhp by a hospital.

It is therefore essential to ensure that the individuals concerned in the hospital are aware of the agency's mission so that it is informed of any incidents which occur, irrespective of the medical device involved and of where it is used in the hospital. In parallel with this action on a specific device, the Dispensing Division has also conducted inspections which have culminated in the withdrawal of nonconforming medical devices.

This plan has a clear purpose: to increase the quality, safety and efficacy of medical devices and to withdraw any devices that do not meet the minimal European requirements.

Informing, teaching, making aware

Since famhp's mission has an educational component, seven additional inspectors have been tasked with reminding the various contact persons of the key aspects of the legislation on medical devices. Using simple documentation, famhp endeavours to make the contact persons aware of the factors to consider with regard to the conformity and quality of the medical devices for which they are responsible in their various storage locations. For example: the importance of CE marking, how to be sure that a medical device conforms, what you need to know when checking the conformity of a medical device ...

This training in the theoretical aspects is followed by an inspection of the hospital pharmacy, care units and surgical suites, in which the medical devices are analysed and checked to ensure that they conform to the regulatory requirements. The inspection also considers their storage conditions and, for implantable medical devices, their traceability.

Following on from the inspections, procedures are implemented to check the medical device take-up process. Awareness campaigns have also been and will be arranged within certain hospitals for the benefit of the personnel concerned (stores personnel, persons responsible for taking up devices, nurses, etc.).

Every approved hospital in Belgium shall be inspected in 2016, with a view to meeting all the contact persons concerned by the various classes of medical device. The aim of these inspections is to ensure that all the individuals who deal with medical devices within hospitals are more familiar with famhp and the work it does. The inspections increase the awareness of the sector overall, for the benefit of every hospital patient.

The inspections increase the awareness of the sector overall, for the benefit of every hospital patient.

Further increases to the scope of the inspections

Clearly, the inspection of premises where medical devices are dispensed is not confined to hospitals. In 2016 and in the future, the Dispensing Division shall also focus on opticians, private general hospitals and dentists. They will subsequently focus on periodontologists, orthodontists, stomatologists, ophthalmologists, dermatologists and private clinics in which surgical procedures are performed.

And not forgetting medical devices dispensed in retail pharmacies

Although the PMH-PDM focuses on implantable medical devices – which are rarely dispensed from a retail pharmacy – the agency nonetheless has a role with these retail pharmacists since they dispense, on a daily basis, many other medical devices such as bandages, sticking plasters, contact lens solutions, condoms, pregnancy tests, thermometers, blood pressure monitors, crutches, etc.

In accordance with the Royal decree of 21 January 2009, each pharmacist is responsible for the quality and conformity of everything he/she dispenses and prepares, which includes medical devices.

In order to support and assist the work of pharmacists, in June 2015 famhp published on its website a brochure about dispensing medical devices in retail pharmacies, which provides the pharmacist with information about:

- how to identify a medical device;
- how to check its conformity;
- ensuring compliance with storage conditions and the expiry date;
- the notification of incidents/complaints about medical devices, and
- the applicable legislation.

In the current context of transparency, inspections of specific types of medical devices were performed in pharmacies during the second quarter of 2015. This action was carried out after publication of the brochure and its aim was educational rather than repressive.

During these inspections, special attention was paid to the following:

- Can pharmacy personnel tell the difference between a product that is classified as medical device and a product with another status (e.g. medicine, food supplement or cosmetic)?
- What checks are performed to ensure that the medical devices acquired by the pharmacy conform? If a nonconformity is detected or suspected for a medical device, what steps are taken?
- Are storage conditions and shelf-life requirements met within the pharmacy?
- In the quality manual, in the part relating to the handling of complaints, is there a complaint submission procedure, a complaint handling procedure and a procedure for the removal from sale further to a complaint? Moreover, the familiarity of the pharmacy personnel with these procedures is checked by invoking a scenario whereby a customer reports an incident relating to the use of a medical device.

Generic medicines or brand-name medicines: no difference for your health

In April 2015, famhp, supported by RIZIV-INAMI (the National institute for sickness and disability insurance), launched an awareness campaign focused on emphasising the quality, safety and efficacy of all medicinal products, both generic and brand-name.

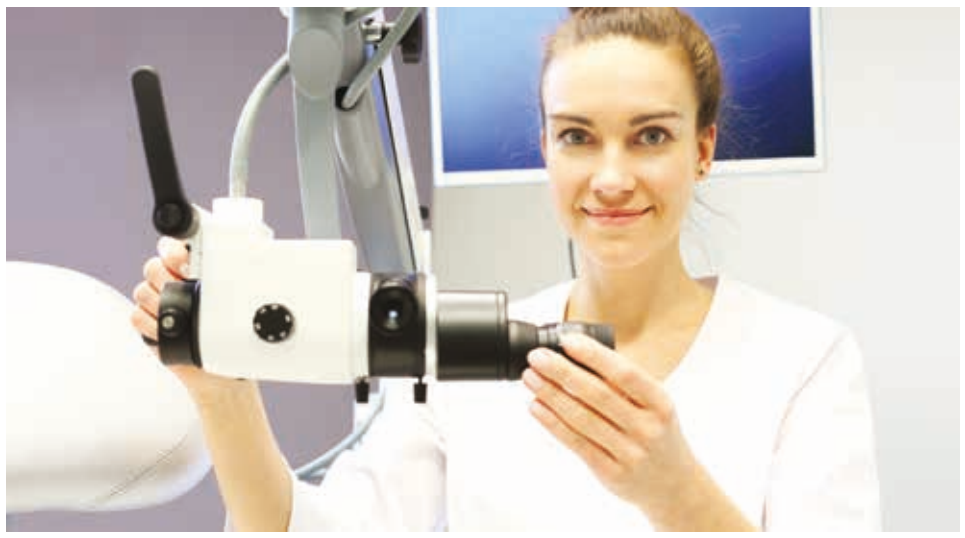
The misperception that generic medicines might be of inferior quality or simply poor imitations persists in the Belgian population. The aim of the campaign was to remind the general public that generic medicines are an equivalent alternative to brand-name medicines.

Via posters in medical doctors' offices and in retail pharmacies, radio adverts, a leaflet and a campaign website, famhp's clear message was that the most rigorous investigation will not detect any difference for your health between a generic and a brand-name medicine. They are both high-quality, safe and effective products.

For more information about generic medicines, about how they are prescribed, how they may differ from brand-name medicines, and for all other information about switching from one medicine to another, visit the website: www.infogenerischegeneesmiddelen.be - www.infomedicamentsgeneriques.be.

A network of materio-vigilance contacts

Materiovigilance monitors the safe use of medical devices. This responsibility is discharged by performing a number of actions, including: collecting and evaluating information and, if necessary, taking corrective measures.



As announced in the annual report 2013, one of the tasks set for the Materiovigilance Entity was to create a network for the collection and dissemination of materiovigilance-related information. The materiovigilance point of contact network has now been put in place and has, since 17 February 2015, become a legal obligation* for hospitals and distributors of medical devices.

Specific tasks for contact persons

The tasks incumbent upon points of contact within hospitals are as follows:

- pass on information about incidents immediately to the distributors and/or manufacturers or to their agents, and to famhp, in accordance with the procedures published on famhp's website;
- participate in the investigations initiated by famhp and in the work relating to the safe use of medical devices;
- record every incident or risk of an incident caused by a medical device, and evaluate them in accordance with the procedure published on the famhp website;
- pass on, if applicable, the measures to be taken following the notification of an incident;
- make all users aware of materiovigilance issues;
- circulate information to the users concerned by an incident.

The materiovigilance points of contact for distributors must:

- pass on information about incidents to the manufacturers or to their authorised agents and to famhp;
- participate in the investigations initiated by famhp and in the work relating to the safe use of medical devices (corrective actions requested in the context of an FSCA (Field Safety Corrective Action), etc.);
- assess, in accordance with the procedure in force, and record every incident or risk of an incident which might be caused by a medical device;
- pass on, if applicable, the measures to be taken following the declaration of an incident;
- make all personnel aware of the materiovigilance issues;
- circulate the information received to the persons and institutions affected.

The contact person is very important since he/she facilitates simpler and quicker exchanges of information with famhp or with manufacturers which improves the levels of responsiveness and effectiveness if, for example, a device has to be quarantined (temporarily or not).

More effective dissemination of information

Over the last few months, a number of letters have been sent to the materiovigilance points of contact within hospitals to make them aware of various issues. By doing so, famhp has been able to inform healthcare professionals of potential issues associated with the use of medical devices.
This special link which famhp is trying to build with the points of contact will be a vital component in the development of materiovigilance in Belgium over the coming years.

** Article 11, § 2bis of the Royal decree of 18 March 1999 on medical devices and article 12, §2bis of the Royal decree of 15 July 1997 on active implantable medical devices.*

Contact | *Some useful information*

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famhp
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This annual report is available in French, Dutch and English.
An electronic version of this 2015 report is available on famhp's website (www.famhp.be).

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