CBG MEB

MEDICINES EVALUATION BOARD

Annual report 2023

Opportunities for tomorrow

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Preface

The year 2023 was an anniversary year for the Medicines Evaluation Board (MEB), as it was exactly 60 years since the organisation was founded. Naturally, we celebrated this in appropriate fashion. However, 2023 was mostly a year of looking ahead. Secretary/director Paula Loekemeijer and chair Ton de Boer discuss the opportunities for tomorrow.

The field of medicine has been undergoing significant changes lately. That is why the title of the MEB Day 2023 was 'Environment in motion'. One of the major themes of the day was the new European pharmaceutical legislation, which was discussed at length with the audience. 'After completely reforming the regulation of veterinary medicinal products in 2022, we started preparing in 2023 for the introduction of the proposed new European legal framework for medicinal products for human use. The new legislation is definitely going to have an impact on our operations and our workload,' Paula says.

'And that is not the only issue at play,' Ton adds. 'Just look at the rapid developments around cancer drugs and other new treatments for increasingly specific, smaller patient groups. At the same time, we also have to deal with the complex and widespread problem of medicine shortages, which is heavily affecting patients, pharmacists and physicians.'

To keep up with all these developments, the organisation will take several steps. 'Internally, we want to make strides in the way we handle our information, for example by starting to work on the basis of data rather than documents containing information. That is why, in 2023, we launched a major project to replace our dossier system for the assessment of medicinal products. This should make us more future-proof, help bring us in line with new developments and curb workloads. A big project for the coming years, which hopefully will benefit us greatly.'

'Connectedness' is one of our core values. We want to do our work in connection with all parties in the medicinal products chain. This helps us keep abreast of upcoming developments and allows us to respond to changes more effectively. That core value was very important to Paula in 2023: 'We are explicitly seeking cooperation, both externally and internally. With the new organisational structure, for instance, we have taken steps to improve our internal cooperation further. The fact that this cooperation has grown stronger was also evident in the annual ISO audit, as a result of which our certification was renewed again. The auditors specifically mentioned the smooth internal cooperation. That makes me proud!'

Another point of pride for Paula and Ton is our international role. Paula: 'We are still doing a lot of work within the European network of medicinal products authorities. We are well represented in the various European committees. The agency is well equipped to allow colleagues involved in centralised European and other procedures to perform their work well. The MEB acts as a strong substantive sounding board for them.'

Ton can attest to that, citing the arrival of three new MEB members in 2023 as evidence. 'We have two new MEB members with backgrounds in oncology and in Advanced Therapy Medicinal Products (ATMPs:

medicinal products with human genes, cells or tissue as a basis – ed.), Annemiek Walenkamp and Anna de Goede. Their expertise is a very welcome addition. Although cancer drugs are assessed at the European level, we do share our expertise with European representatives. This makes having more in-house knowledge highly valuable. Moreover, ATMPs form one of the MEB's scientific themes, as we expect them to play an increasing role in society in the coming years.'

In addition, society now has another voice on the MEB. 'Our third new MEB member, Carina Pittens, conducts research into patient participation in her daily work. Thanks to her, the voice of patients and their loved ones will again be more strongly represented on the MEB,' Ton believes.

In that sense, a lot has happened since tiger balm received its first marketing authorisation number (RVG number) 60 years ago. 'In 2023, we went through many tens of thousands of registrations and expanded the scope of our role, for example by encouraging the proper use of medicinal products and providing reliable information about them,' Ton explains. 'I think a great example is the campaign around contraceptives in the autumn. We noticed that all kinds of stories about contraception were circulating on social media like TikTok and Instagram – stories which were not always accurate or complete. Through the campaign, we delivered the message that women and young girls should use reliable sources of information for their contraceptive choices.'

Such campaigns, which highlight the MEB's commitment to sharing reliable information on medicinal products, are important. 'The reputation survey we commissioned in 2023 shows that people consider the MEB competent, scientific, reliable and independent. This is positive, because it helps us in our work. It is important to maintain that good reputation.'

A changing medicine landscape, medicine shortages, a new assessment system and the arrival of new legislation offer opportunities for tomorrow in all sorts of areas!

Ton de Boer, chair
Paula Loekemeijer, secretary/director

The MEB in 2023

The year 2023 was all about anticipating and preparing for change. Highlights included new European legislation, increasing involvement in European procedures, stepping up cooperation to reduce medicine shortages and developing accessible product information for patients and care providers. These are topics that employees the Medicines Evaluation Board Agency (MEB Agency) deal with every day. Below, we take a look back with some of them.

Focus on Europe

Peter Mol, senior assessor at the MEB Agency, has been a member of the CHMP, the EMA's committee for medicinal products for human use, since August 2023. This is a challenging role, in which he represents the Netherlands together with alternate CHMP member Patrick Vrijlandt.

'We receive considerable support and input from the organisation. This year also saw the launch of a core team at the MEB Agency, which has taken over substantive and organisational tasks from us as CHMP members. This is very nice, because we play a big role in Europe and this allows us really to focus on the content,' Peter says.

More and more new medicinal products are registered through a centralised procedure, Peter explains. 'The number of cancer drugs is increasing, while we are also seeing more and more personalised medicinal products. Also, applications for generic medicinal products are now going through centralised procedures more often.' That European trend is expected to continue. The growing number of centralised procedures and the large Dutch involvement in them does lead to a need for greater focus. 'We need to start making choices in the coming years about specific areas where we see a role for ourselves – for instance, in areas where we already have the necessary expertise in-house. An example of this is the use of real-world data to get more information about the efficacy and safety of medicinal products.'

"The MEB is a very good sounding board for the discussions we are having in Europe."

Although centralised procedures go through the European system, the MEB plays an important role there too. 'The advice from the MEB is highly valuable. It is a very good sounding board for discussions we are having in Europe. We can really build on the expertise from the field that the MEB members contribute.'

New European legislation
In the future, there will be drastic changes to the way we allow medicinal products on the market in Europe. This is because there is a proposal to review the European legal framework for medicinal products for human use. The MEB Agency is preparing for this new legal framework, which will involve working in a changing environment.

Regulatory Project Leader (RPL) Rosalinde Bot knows a lot about this. 'Besides my role as RPL, I started working as a liaison with the Ministry of Health, Welfare and Sport in 2023. For half a year, me and a colleague, formed the linking pins between the Ministry and the MEB Agency to ensure that the Ministry has substantive input on changes that are important to the MEB.'

The proposed European legal framework needs this Dutch input. 'Whereas the Ministry of Health, Welfare and Sport looks at the proposal mainly at the policy level, we look at whether the legislation is enforceable, among other things,' Rosalinde says.

"The result will be a future-proof, sustainable way in which we can regulate medicinal products at the European level."

'Our subject-matter experts look at all statutes in the proposed legal framework. Do we foresee substantive or practical problems in implementation? What is our position? What impact will this have? Of course, we also take a close look at where there are difficulties, or where we see opportunities to improve the proposal. As liaisons, we coordinate all that information to deliver it to the Ministry.'

Numerous components and statutes of the proposed legal framework were considered in 2023. Still, it is and remains a long and complex process, Rosalinde says. 'Things are constantly changing again, as new insights or different opinions keep coming from any one of the 27 countries. In 2024, this will continue in full force. It is a time-consuming process. However, the result will be a future-proof, sustainable way in which we can regulate medicinal products at the European level.'

Working together to reduce medicine shortages

We are also joining forces at the European level to deal with medicine shortages. Hanneke Mulder, medicine shortages expert: 'The new European legal framework is a great example of this. Medicinal products authorities and manufacturers will have more duties and responsibilities to combat

shortages as a result. This will soon require them to gain a more thorough understanding of where vulnerabilities lie in the supply chain and to have an action plan ready for when a problem arises. In 2023, we also published a European list of critical medicinal products. Keeping the medicinal products on this list available will become a priority within Europe.'

"Any shortage is something we need to avoid, whether the medicinal product in question is on the critical list or not."

However, any shortage is something we need to avoid, whether the medicinal product in question is on the critical list or not. The need to intervene more frequently in 2023 is apparent from the recently published **annual report** of the medicine shortages and defects notification centre. Hanneke confirms this: 'We are seeing an increase in the number of granted requests for Temporarily Different Packaging and the number of shortage decisions issued by the Health and Youth Care Inspectorate (IGJ).' How do those shortfalls occur? 'Often, the cause lies with production or distribution problems. However, an increase in demand can also be behind it. In 2023, the diabetes medicine Ozempic was a good example. The rise in demand is suspected to be due to off-label use to lose weight. The popularity of this off-label use may also be due to the attention it received on social media from celebrities at home and abroad.'

'Of course, we realise that the solution to the problem of medicine shortages is not simple. We remain committed to minimising the impact of shortages on patients,' Hanneke says.

The role of digitalisation

Data is taking on an increasingly prominent role in the world of medicinal products and their assessment. Data-driven working methods help us assess medicinal products and monitor adverse reactions, but digitalisation can also help with sharing information.

The electronic product information (ePI) project is an example of this. Erol Hofmans, ePI project manager at the MEB Agency: 'ePI is designed to make medicinal product information more accessible. Also, ePI makes it easier to keep medicinal product information up to date, for both patients and care providers.'

'In 2023, we launched pilots with the EMA and medicinal products authorities in Spain, Sweden and Denmark. In addition, several companies from all overarching groups – innovative, generic and self-care – are participating in these pilots. Together, we look for the best solutions,' Erol says.

"ePI is designed to make medicinal product information more accessible."

‘In November 2023, the first ePI was published. An important milestone! Also, the introduction of ePI in a European legislative proposal shows that we are on the right track,’ says Erol. ‘A great starting point to move forward with in 2024.’

The year in a nutshell

A lot of events took place in the year 2023. Some highlights are described below. The year 2023 in a nutshell.

January

20 January

Publication of research into self-care medicinal products

The results of the survey on the proper use of self-care medicinal products are published. Users have limited information needs about self-care medicinal products, and their usage could be improved.

March

7 March

Publication of the annual report of the medicine shortages and defects notification centre

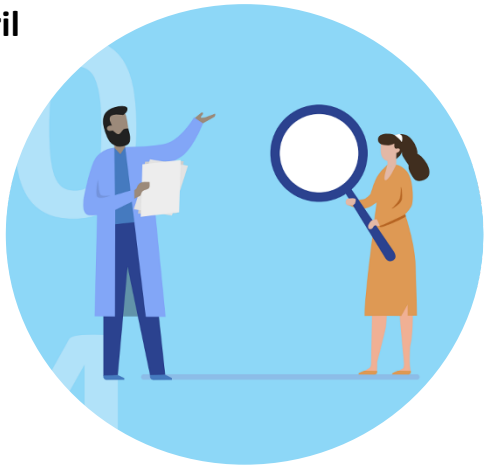
The annual report of the MEB and the IGJ for 2022 shows that more action had to be taken that year to address long-term shortages than in the previous year.

17 March

MEB warns of ongoing shortage of diabetes medicine Ozempic

The off-label use of Ozempic as a weight-loss drug has earned it considerable media attention. This creates shortages for diabetes patients.

April



13 April

MEB Science Day and publication of the science brochure

The MEB Science Day is held at the Jaarbeurs in Utrecht, with a theme of 'Biomarkers and Companion Diagnostics – The future of precision medicine'. Simultaneously, the science brochure 'Towards Tomorrow' is published. This brochure provides an update on regulatory science activities in light of the MEB's Science Policy 2020–2024.

June

14 June

MEB Day

Over 500 visitors attend the MEB Day at DeFabrique in Utrecht. Through the theme 'Environment in motion', they learnt all about the changing world of medicine.

22 June

Publication of the State of Implementation

The State of Implementation, the government-wide programme to improve public services, is published. For the MEB Agency, the focus is on trust in medicinal products and vaccines. The main themes in the State of Implementation are pressure on the European system and the MEB Agency, the availability of medicinal products, reliable information and transparency, and the changing environment.

July

5 July

No reason to change legal status of supply of self-care medicinal products

At the request of the Minister of Health, Welfare and Sport, the MEB conducted research into the classification of self-care medicinal products. This was triggered by concerns about the correct classification of different self-care medicinal products after plans for the amendment of the law to include digital information. The MEB concludes that there is no reason to change the legal status of supply of self-care medicinal products.

September

26 September

Campaign for World Contraception Day

On World Contraception Day, we launched a campaign to make people aware of the disinformation about contraception on the Internet. MEB's message: always make your choice based on reliable sources, and see your GP if you have any questions. Several national and regional media outlets took up the MEB's message.

October

24 October

Emer Cooke visits the MEB

Emer Cooke, executive director of the European Medicines Agency (EMA), visited the MEB. Topics discussed included international cooperation and the changing world of medicinal product assessment.

November

6 November

International Medicines Safety Week

The theme of this year's International Medicines Safety Week is 'anyone can make a report'. We pay attention to the roles of different target groups in reporting adverse reactions.

8 November

Publication of the first electronic product information (ePI)

As part of a European trial, the MEB publishes the first electronic versions of product information (ePI). Electronic product information improves the usability of medicinal product information and makes it more accessible to all users, such as care providers and patients.

Medicinal products and vaccines for human use[1]

Rapporteurships and co-rapporteurships assigned to the Netherlands through the centralised procedure (CHMP)

The responsibilities of the Committee for Medicinal Products for Human Use (CHMP) include assessing centralised applications for marketing authorisations for medicinal products. Of the nearly 100 centralised procedures received by the EMA in 2023, the MEB Agency was involved as rapporteur or co-rapporteur in one-fifth of them.

In 2023, the Netherlands was rapporteur fewer times than in 2022. However, the Netherlands was more often involved in centralised procedures as co-rapporteur in 2023. In total, the Netherlands was rapporteur 10 times and co-rapporteur eight times (compared to 17 and five times respectively in 2022). While the number of rapporteurships has decreased somewhat over the years, the dossiers are much larger and more complex.

In 2023, Germany was awarded the most rapporteurships and co-rapporteurships. Austria followed in second place. Sweden, the Netherlands and France completed the top five. There were five countries that were not assigned rapporteurships or co-rapporteurships.
See Table 1.1a in the appendix for the number of rapporteurships and Table 1.1b for the European overview.

More European cooperation

The MEB Agency has an important role in Multi National Assessment Teams (MNATs). In these teams, several countries tackle a rapporteurship together. This also gives countries with less experience in rapporteurships the opportunity to gain experience. MNAT partnerships promote European cooperation. They also help the MEB Agency manage its very high workload, especially in the area of quality assessment.

Of the 18 CHMP rapporteurships and co-rapporteurships assigned to the MEB Agency in 2023, five were assigned as MNATs. In most cases, the participating country took responsibility for assessing the quality aspects of the medicinal product in the MNAT.

Assigned pharmacovigilance rapporteurships (PRAC)

The Pharmacovigilance Risk Assessment Committee (PRAC) plays an important role in monitoring the risks of medicinal products for human use in Europe. The PRAC provides recommendations to the CHMP and the Coordination Group for Mutual Recognition and Decentralised Procedures human (CMDh) on the risks of medicinal products that have been or will be authorised in the European Union. In 2023, the MEB Agency was allocated slightly fewer PRAC rapporteurships than in the

[1] This chapter does not consider herbal medicinal products and homeopathic products. These products are discussed in a separate chapter: Botanicals and novel foods.

previous year. Of the 14 PRAC rapporteurships assigned to the MEB Agency in 2023, 11 were for new active ingredients and three for biosimilars.

With 14 PRAC rapporteurships, the MEB Agency continues to have a leading role within Europe. Germany was allocated the most rapporteurships in 2023, followed by Sweden and the Netherlands. In the European context, the MEB Agency is also responsible for pharmacovigilance of 101 active ingredients. This means that, for these ingredients, the MEB Agency is responsible for analysing data in the European database of suspected adverse reactions (Eudravigilance database) and for identifying signals of possible new or changed risks. Table 1.2a in the appendix shows the number of PRAC rapporteurships, while Table 1.2b shows the distribution of PRAC rapporteurships across Europe.

Applications submitted through the decentralised procedure (DCP) and the mutual recognition procedure (MRP)

The number of initiated procedures for which the Netherlands was the Reference Member State (RMS) was 236 in 2023. This was more than in 2022, when 180 procedures were initiated. In 2023, Germany was the RMS for the most DCP applications, followed by the Netherlands. The Netherlands was the RMS for the most MRP applications. See Tables 1.3a and 1.3b in the appendix.

Applications through the national procedure

The number of applications submitted through the national procedure (excluding parallel imports, including duplex marketing authorisation procedures) continues to fluctuate between 60 and 80 per year. See Table 1.4 in the appendix. Most applicants prefer a European procedure (centralised and decentralised), which allows the product to receive marketing authorisation in several European countries simultaneously.

National applications for parallel imports

There were 224 applications for parallel import marketing authorisations in 2023, down from 302 in 2022. See Table 1.5 in the appendix.

Number of registered marketing authorisations and withdrawals following registration

In 2023, a total of 13,774 marketing authorisations were registered in the Netherlands. That number was similar to the previous year.

When a company makes a request for withdrawal of the marketing authorisation, the MEB (Agency) looks at whether it is a critical product. For example, if there are no similar medicinal products in the same medicinal product group, the MEB (Agency) will investigate what options are available to keep the product on the market for Dutch patients. The MEB (Agency) does this in consultation with the marketing authorisation holder.

The year 2023 saw a slight decrease in the number of marketing authorisation withdrawals.
See Tables 1.6a and 1.6b in the appendix for an overview of registered and withdrawn marketing authorisations.

Scientific advice

By providing scientific advice, the MEB contributes to responsible medicinal product development, innovation and early patient access.

Scientific advice can cover various aspects, such as clinical or toxicological product development, but also regulatory aspects. The advice can relate to the entire product cycle: from pre-clinical research phase to post-marketing change proposals. The advice can provide manufacturers with clarification on the requirements for a complete and valid drug dossier submission. This advice allows manufacturers to determine investment security.
Partly because of this, issuing scientific advice is a statutory duty. There are both national and centralised (European) procedures for issuing scientific advice. As a statutory duty, national scientific advice falls under the direct responsibility of the MEB. Centralised scientific advice is prepared by the European Scientific Advice Working Party (SAWP). This concerns a European consensus under the responsibility of the CHMP. The MEB (Agency) issues both European and national scientific advice. Incidentally, it is not compulsory to request scientific advice.

The number of scientific opinions prepared by the SAWP in 2023 was 109. This is a decrease from the 140 opinions prepared in 2022. See Table 1.7 in the appendix. The decrease was due to the reduced inflow of scientific advice at the European level in 2023.
Since 2022, the MEB has participated in the Simultaneous National Scientific Advice (SNSA) pilot. This type of advice focuses on clinical trials, but other topics are also covered. Applicants can request scientific advice from several EU countries at the same time.

Number of national scientific opinions

The number of national scientific opinions increased slightly in 2023 compared to 2022, from 110 to 114.

The MEB also issues tailored advice, allowing start-ups and academic groups to seek advice at a reduced rate. This encourages innovation at universities and in small businesses. Academic groups in particular were increasingly able to find the MEB for tailored advice in 2023.
See Table 1.8 in the appendix for figures on national scientific opinions.

As in previous years, the MEB was actively involved in *drug rediscovery* projects set up by ZonMw. ZonMw is the Dutch body that promotes and funds health research and innovation. By assessing project applications for research into medicinal products, which are sometimes already used off-label in practice, the MEB contributes to a possible on-label application. There are significant benefits to this for prescribers and patients, but also for pharmacovigilance. This is because the registered application is mentioned in the product information, including in the patient information leaflet.

Adverse reactions

Identifying and assessing adverse reactions to medicinal products is a core task of the MEB. On behalf of the MEB (Agency), the Netherlands pharmacovigilance centre Lareb collects, records and analyses reports of suspected adverse reactions from care providers and patients. Lareb sends relevant findings from these analyses to the MEB.

In 2023, Lareb and the MEB (Agency)discussed 38 analyses of reports of suspected adverse reactions. Of the 38 analyses, 10 were developed for discussion in the MEB meeting and three for discussion by the MEB Agency's Medical Practice Committee. The remaining analyses have found their way into ongoing proceedings at the MEB or are being monitored closely.

Signal detection

In the European context, the MEB Agency is responsible for the signal detection of 101 active ingredients, or combinations of active ingredients. In 2023, the MEB Agency assessed 18 signals in the European context.

As part of the PSUR Single Assessment (PSUSA) procedure, the MEB Agency assesses Periodic Safety Update Reports (PSURs) for these 101 active ingredients. It does the same for all products for which the MEB is a PRAC rapporteur.

A PSUR is a comprehensive and critical analysis of a product's risk-benefit balance. It gives medicinal products authorities updates on global safety experiences with a product at set intervals after registration. The need to submit PSURs is determined using a risk-based approach. The frequency with which PSURs are submitted varies.
In 2023, the MEB Agency conducted 122 PSUSA assessments in the European context.

PASS protocols and study results

If there any remaining uncertainties about the safety of a medicinal product, a company may be asked to conduct additional safety studies, called Post Authorisation Safety Studies (PASS). The MEB (Agency) reviewed 29 protocols and study results last year.

Direct Healthcare Professional Communication

In case of urgent or important safety issues, medical professionals are notified with a letter, called a Direct Healthcare Professional Communication (DHPC).

In 2023, 14 DHPCs were sent. The MEB Agency is exploring options for sending risk communications, including DHPCs and additional risk minimisation material, digitally. See Table 1.9 in the appendix.

Other activities

International Medicines Safety Week

As in previous years, the MEB and Lareb participated in the International Medicines Safety Week, under the banner 'Working together for safe medicine use'.

Regulatory research

As in previous years, the MEB Agency participated in regulatory research with a focus on pharmacovigilance. There were multiple PhD tracks in 2023. These PhD tracks s can be found in the

Science brochure – Towards Tomorrow. This brochure also describes the scientific activities of the past year with the involvement of the MEB agency.

Student research into switching to different medicinal products

The MEB Agency has set up a student research project to investigate whether and which medication incidents occur as a result of switching to different medicinal products due to medicine shortages. We are carrying this out together with the Dutch Institute for Rational Use of Medicine's project to prevent medication incidents (*Voorkomen Medicatie-Incidenten*, VMI).

Patient Information Network (NPI)

In order to make reliable, understandable and accessible information easily available to patients, the Patient Information Network (*Netwerk Patiënteninformatie*, NPI) was established in 2018, together with the Dutch College of General Practitioners (NHG), the Royal Dutch Pharmacists Association (KNMP) and Lareb. The members of this network meet regularly.

They undertake activities to make comprehensible information available together. A multi-year work plan has been drawn up for this purpose. Several results have emerged from the network's activities. Examples include a writing guide for promoting the comprehensibility of patient information leaflets, short summaries of vaccine information (Vaccine in a nutshell) and animated videos on COVID-19 vaccinations. In 2023, the NPI celebrated its fifth anniversary. In addition, Stichting KIJKsluiter became a candidate member of the NPI.

Furthermore, 17 parties from the medicinal product information landscape signed a letter of intent on 8 December 2022. These include BOGIN, VIG, VES, Neprofarm, CBD, KNMP, MEB and the Ministry of Health, Welfare and Sport. The aim of this partnership is to develop a new, uniform set of icons. The use of uniform icons in medicinal product information contributes to greater understanding, better and safer use of medicinal products and greater compliance. This led to the publication of the first set of icons in January 2024. The remainder will be published later in 2024.

Botanicals and novel foods

The Botanicals and Novel Foods (BNV) team has two tasks. The first is the assessment of herbal medicinal products and homeopathic products. The MEB makes marketing authorisation decisions for these groups of products as well.

In addition, the team provides policy support to the Ministry of Health, Welfare and Sport (VWS) in the authorisation of novel foods, pursuant to the EU Novel Foods Regulation. Since 2018, this has been done within a European system based on assessments by the European Food Safety Authority (EFSA). The Ministry of Health, Welfare and Sport decides on authorisation for the Netherlands.

The BNV team also represents the Netherlands on the EMA's Herbal Medicinal Products Committee (HMPC). The HMPC reviews scientific data on herbal medicinal products and compiles European herbal monographs.

Number of marketing authorisations for herbal and homeopathic medicinal products

The number of herbal medicinal products with a marketing authorisation on the Dutch market has been slowly decreasing in recent years. In 2023, the number of authorisations for herbal medicinal products decreased slightly. See Table 2.1 in the appendix. This is probably due to the simultaneous availability on the market of herbal products, which are regulated as supplements under the Commodities Act. These herbal products have not been assessed by the MEB for quality, safety and efficacy. This remains a confusing situation for consumers.

In 2023, three new herbal medicinal products were registered. Of these, two were registered through the decentralised procedure, with registration based on an assessment by an RMS. The MEB can simply adopt such assessments. The HMPC's herbal monographs play an increasingly important role in this.

The total number of marketing authorisations for homeopathic medicinal products (2,044) has remained stable over the years. See Table 2.2 in the appendix.

Veterinary medicinal products

The MEB Agency's Veterinary Medicinal Products Unit (VMPU) handles and assesses applications and issues production, distribution and marketing authorisations for veterinary medicinal products. The VMPU advises the Ministry of Agriculture, Nature and Food Quality (LNV) on this matter through the Committee for the Authorisation of Veterinary Medicines (Ctd). In the Netherlands, the Minister of Agriculture, Nature and Food Quality is responsible for the marketing authorisation of veterinary medicinal products.
The VMPU is also tasked with monitoring the adverse events of veterinary medicinal products, granting trial exemptions for veterinary medicinal products and feed additives, and issuing batch approvals for veterinary vaccines, export certificates and licences for wholesale and retail trade.

Inspections

Since January 2019, the MEB Agency has taken over veterinary pharmacovigilance inspections from the IGJ. In 2023, the VMPU conducted three pharmacovigilance inspections.

Assigned centralised CVMP rapporteurships and co-rapporteurships

In 2023, the MEB Agency was assigned one co-rapporteurship by the Committee for Veterinary Medicinal Products (CVMP). The number of co-rapporteurships has been stable over the years – 2021 was an outlier. The number was high in that year because most of the rapporteurships were part of a bundle of rapporteurships. See Table 3.1 in the appendix.

Assigned centralised MRL rapporteurships and co-rapporteurships

For substances used as medicinal products for food-producing animals, a maximum residue limit (MRL) must be set. The rapporteur for an MRL application assesses the maximum safe concentration of the residue of an active ingredient in the various consumable products of animal origin. In 2023, the MEB Agency was assigned one MRL rapporteurship/co-rapporteurship. See Table 3.2 in the appendix.

Closed RMS applications through the mutual recognition and decentralised procedure

In 2023, the Netherlands closed 50 DCP applications as an RMS. This number was higher than in the previous year. The share of the European work carried out by the Netherlands is large: the Netherlands closed the most RMS applications in 2023. See Tables 3.3a and 3.3b in the appendix.

Number of marketing authorisations and number of withdrawals of marketing authorisations

Last year saw a very slight decrease in the number of marketing authorisations for veterinary medicinal products registered in the Netherlands – 2,246 in 2023 compared to 2,279 in the previous year.

In addition, 2023 saw a slight increase in the number of withdrawals of marketing authorisations for veterinary medicinal products at the request of the marketing authorisation holder: 153 (compared to 143 in 2022).
See Tables 3.4a and 3.4b in the appendix for the number of marketing authorisations and withdrawals.

Governance and organisation

Organisational structure

The MEB is an autonomous administrative authority within the central government of the Netherlands. The MEB makes decisions on the authorisation of human medicinal products on the Dutch market and assesses the safety of novel foods for consumers. As an independent authority, the MEB regulates the quality, effects and safety of medicinal products and promotes the proper use of medicinal products for the right patient.

The MEB provides scientific advice and is responsible for the classification of medicinal products (legal status of supply) and pharmacovigilance. Furthermore, the MEB gives advice on medicinal products incorporated in medical devices. The preparation and implementation of decisions of the MEB are carried out by the MEB Agency, which is headed by the MEB Agency director/MEB secretary.

MEB

The MEB has a maximum of 17 members, including the chair. The members are medical specialists, hospital pharmacists, professors and other experts. MEB members are appointed by the Minister of Health, Welfare and Sport for a period of four years. Members can be reappointed twice.
In 2023, two MEB members stepped down: Henk-Jan Guchelaar, hospital pharmacist, and Rob van Marum, geriatrician.

Three members joined the MEB in 2023: Anna de Goede, hospital pharmacist with expertise in ATMPs; Carina Pittens, MEB member with expertise in patient and consumer perspectives; and Annemiek Walenkamp, MEB member with expertise in oncology.

In principle, a meeting attended by all MEB members takes place once a month, while another monthly meeting is attended by a smaller group of members. In addition, a rotating group of MEB members meets once a month to discuss dossiers specifically related to pharmacovigilance. The chair and vice-chairs also meet with agency employees once a week to discuss specific questions about medicinal product dossiers. Furthermore, MEB members are regularly consulted in assessment work on an ad hoc basis. For the MEB's statutory duty with regard to issuing scientific advice, a coordination meeting takes place in the presence of the chair of the MEB every two weeks.

Agency

The MEB Agency supports the MEB. Administratively, the agency falls under the Ministry of Health, Welfare and Sport. Substantively, it falls under the authority of the MEB as far as tasks for which the MEB is responsible are concerned. The agency is responsible for preparing and implementing decisions by the MEB. The agency handles some 20,000 cases annually. Those cases range from administrative changes to reviews of medicinal product dossiers with new active ingredients.

On 1 February 2023, the agency's organisational structure was changed to a divisional structure with three divisional heads and a managing director. The departments fall under three divisions:

1) Assessments & Marketing Authorisation

2) Europe, Medicine Use & Veterinary Medicinal Products
3) Business Operations, Legal Affairs & Communications

During the reorganisation process, explicit consideration was given to the embedding of the group of European representatives (highly specialised employees representing the Netherlands in the EMA's crucial committees). In addition, employees from the MEB Agency serve as Dutch representatives in European committees.

European representation

The Netherlands is represented in the EMA's European scientific committees. The Dutch committee members are part of the agency.

At the CHMP and the PRAC, the lines for the assessment of medicinal products for human use under the European centralised procedure converge. These committees include representatives from all EU countries. The committees meet monthly at the EMA in Amsterdam.
If the Netherlands is rapporteur, a team of MEB Agency employees assesses the dossier. The composition of the team depends on the medicinal product and the topics to be answered in the assessment. The team then submits the results of the assessment to the MEB. The MEB, together with the European committee members, will recommend a proposal that the Dutch CHMP or PRAC members can take into the discussion with the committees.
For the allocation of rapporteurships and co-rapporteurships, the EMA uses criteria whereby allocation is based on the best available expertise in the Member States, while leaving room for countries that have been less frequent rapporteurs in the past.
The allocation of co-rapporteurships is different at the PRAC than at the CHMP: the country that is CHMP rapporteur automatically becomes PRAC co-rapporteur.

Besides the CHMP and the PRAC, the EMA has four other scientific committees to advise on the centralised procedure for medicinal products for human use:

- the Committee for Orphan Medicinal Products (COMP)
- the Paediatric Committee (PDCO)
- the Herbal Medicinal Products Committee (HMPC)
- the Committee on Advanced Therapies (CAT)

Several working groups are active within each EMA scientific committee. An example of this is the SAWP.

The coordination of European work on decentralised and mutual recognition procedures has been assigned to the CMDh. The CMDh is a scientific committee of the Member States, but like the other committees, it meets at the EMA and is also supported by the EMA.
The EMA's HMPC reviews scientific data on herbal medicinal products and produces European herbal monographs.
The CVMP is the EMA's scientific committee for veterinary medicinal products. All EU Member States have representatives on this committee.

Analogous to the CMDh for human medicinal products, there is also a group coordinating European work on DCP and MRP procedures for veterinary medicinal products: the Coordination Group for

Mutual Recognition and Decentralised Procedures veterinary (CMDv). The Dutch representatives on both the CVMP and the CMDv work at the VMPU.

The Advisory Board

The task of the Advisory Board is to advise the MEB independently and critically about the major policy themes and other aspects of our tasks. It provides advice by focusing strategically on the environment in which the MEB operates.

In 2023, the Advisory Board advised on the multi-year strategy and the review of the European pharmaceutical legislation.

Transparency, independence and integrity

As an autonomous administrative authority, the MEB aims to make independent, reasoned and insightful decisions. That is why the MEB publishes minutes of council meetings and when the MEB makes a decision, provides an opportunity to submit opinions and be heard. A person can also object to an MEB decision and then appeal to the courts.

Independence demands integrity. The MEB Agency safeguards integrity with a Code of Conduct and an integrity policy. MEB members, MEB Agency employees and external experts complete a 'declaration of interests'. This is done prior to employment or when entering into a contract. After the first time, this happens annually. New interests should be reported in the interim.

Objection and appeal procedures

In 2023, 23 different objection and (higher) appeal procedures were pending. The procedures could be broadly divided into two main categories; see Table 4.1 in the appendix. The first category includes procedures in which decisions to grant or refuse a marketing authorisation were at issue. The other category covers procedures on disclosure decisions under the Open Government Act (*Wet open Overheid*, Woo). In both types of procedures, competitive interests of pharmaceutical companies play an important role.

Requests under the Open Government Act (Woo)

In 2023, the MEB received a total of 37 disclosure requests under the Woo. In most cases, such requests are made by competing pharmaceutical companies. The vast majority of requests were about pending applications for marketing authorisations before the MEB.

The MEB Agency also handles Woo requests relating to veterinary medicinal products. We do this on behalf of the Minister of Agriculture, Nature and Food Quality. One Woo request pertaining to a veterinary medicinal product was received in 2023.

Opinion procedure

If the MEB intends to take a negative decision, interested companies (such as the applicant or competitors) have the opportunity to submit an opinion. An opinion procedure can be either written or oral. In 2023, the MEB processed 11 opinions. See Table 4.2 in the appendix.

Quality management

The MEB Agency has been ISO-9001 certified since 2006. With this certificate, the MEB Agency shows that it complies with this international standard in the field of quality management for the performance of its statutory duties.

For its statutory pharmacovigilance duties, the MEB Agency is required by European regulations to operate a quality system. Although external certification is not, strictly speaking, mandatory from a regulatory perspective, the MEB Agency considers it important to adopt a transparent and, where possible, verifiable approach. External certification helps with this. The 2023 audit certification shows that the MEB Agency continues to meet the standard.

Complaints

In 2023, six complaints were received from external parties. Of these, one was upheld, one was declared unfounded, one was partially upheld and three were declared inadmissible. No systematic underlying causes have been identified.

Use of open standards and open source

Compliance with open standards rules, such as information security, digital accessibility and openness, touches on several domains of the MEB Agency, including quality management, procurement and information management. In line with the civil service instructions for purchasing ICT products and services (*Instructie Rijksdienst*), the MEB Agency uses the Netherlands Standardisation Forum's list of open standards when acquiring or realising new information facilities. This involves assessing which open standards apply to information provision in the initial phase and setting them down as requirements for the implementation of this provision. If there is any deviation from the civil service instructions, this will be stated with reasons. At the MEB Agency, there was no deviation from the civil service instructions in 2023.

Facts and figures

At the end of December 2023, the MEB Agency had 511 employees. Together, they accounted for 474.7 FTEs on average. See Table 4.3 in the appendix. In 2023, the workforce was 68% female and 32% male. Women held 54% of executive positions. The average MEB Agency employee is 43.7 years old and works at a part-time rate of 92.9%. The average employee at the MEB Agency has 8.2 years of service.

The average sickness absence rate for 2023 was 4.6%. This was similar to the previous year.

Diversity & inclusion

The MEB Agency's ambition is to be an inclusive employer, which includes being accessible to people at a distance from the labour market. The legal frameworks for this are laid down in the Participation Act and the Occupational Disability (Employment Targets and Quotas) Act.

The goal for the MEB Agency was to create a total of 17.4 jobs for people at a distance from the labour market in 2023. Of these, 14.2 jobs were filled in 2023. Through intensified cooperation with the Ministry of Health, Welfare and Sport and increased focus on this topic, we managed to fill more jobs than in the previous year.

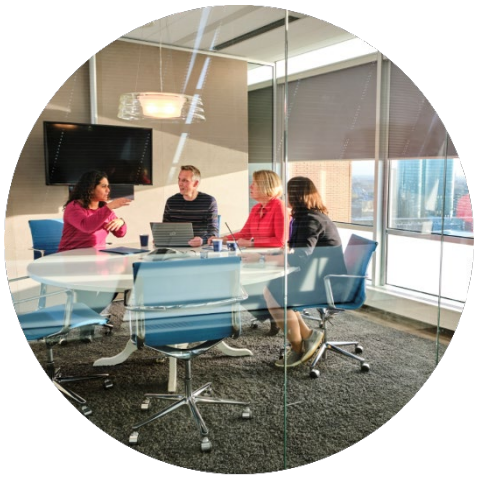
The Diversity & Inclusion working group of the MEB Agency grew in 2023. Several colleagues joined, and the internal working group consisted of six employees in December 2023. The working group raises awareness by organising activities and sharing viewing and listening tips. In addition to raising awareness, the working group is also looking at minimising gender designation, for example in systems used by the MEB Agency.

Accommodation

In July 2023, it was announced that the MEB Agency stays at the Graadt van Roggenweg in Utrecht. In 2022, the MEB Agency would relocate, but in 2023, it was confirmed that the MEB Agency remains in Utrecht.

Information provision

In the area of ICT/information provision, continuity of the current medicinal product assessment system and preparations for a new system were key issues in 2023. Significant progress has been made on both. The continuity of the current ICI system has been greatly improved.



The tender for the new dossier system (Figaro) was launched in 2023, including by holding a market consultation. The aim of this market consultation is both to communicate the needs of the MEB Agency to potential suppliers and at the same time to get feedback from suppliers on the latest market developments, which the tender can then take into account. Publication of the tender is expected in March 2024, followed by the final award in June 2024.

Another important development was the further professionalisation of the portfolio management process. There is an increasing focus on steering the process towards achieving a weighted prioritisation of the functional needs of the business. For this reason, a schedule looking several quarters ahead has been drawn up to provide more clarity for the business in terms of expectations.

Finances

The coronavirus pandemic continued to impact the amount of work at the MEB Agency in 2023. Additional work included monitoring the new and adapted medicinal products to combat the coronavirus. This created an increased workload for employees. To reduce the workload to a responsible level, additional employees were hired. To cover these additional costs, the MEB Agency used the remainder of the Ministry of Health, Welfare and Sport's contribution from previous years (€1.0 million).

Result

The MEB Agency posted a negative result of €2.5 million in 2023. This is explained by a €0.7 million lower income than budgeted and €1.8 million higher costs. The €2.5 million loss can be absorbed using equity.

Income

The €0.7 million lower income compared to the budget can be partly explained by the reduced contribution from the Ministry of Health, Welfare and Sport, which was €1.2 million lower. Income from procedures and annual fees was also €0.6 million lower than budgeted. This was partially offset by interest income of €0.9 million and an additional €0.2 million income (including grant income) from other sources, such as the European Commission (third-party revenue).

The lower contribution from the Ministry of Health, Welfare and Sport is due to a reduced contribution for the Information Management in Order programme. Additionally, fewer costs were incurred for the projects covered by the Work on Implementation (WaU) funds (ICT apparatus and other material costs), resulting in lower revenue as well.

The lower revenue from procedures and annual fees is *on balance* due to higher revenue from centralised procedures (€0.4 million), veterinary medicinal products (€0.5 million) and annual fees (€0.4 million), but lower revenue from decentralised procedures (€1.8 million) and mutual recognition procedures (€0.1 million). The inflow of decentralised procedures in 2023 was as expected. However, the outflow/completion of cases lagged behind, partly due to the high volume of Nitrosamine dossiers and the high workload.

Expenditure

Due to proactive recruitment and the sharp increase in individual choice budget hours saved in 2023, the cost of own staff was €2.1 million higher than budgeted. An amount of €2.0 million was added to the leave balance. The cost of external hiring was €1.6 million higher than budgeted.

As in 2022, it remained difficult to fill vacancies with permanent employees. These included vacancies in ICT for regular work as well as for the various programmes and projects. Due to delays in the implementation of projects and programmes with an ICT component, material costs for ICT devices and ICT depreciation costs were €1.3 million and €0.2 million lower, respectively. As a result, other material costs were lower as well.

Looking ahead to 2024

Because the MEB Agency had to use much of its equity in 2023 to absorb the negative result, there is little financial room left in 2024 to absorb setbacks. Both the revenue and cost sides will be tightly managed to stay within the margin of remaining equity.

In 2023, the decision on the adjustment of the EMA's fee structure (fee regulation) will be finalised. The new fee structure will take effect on 1 January 2025. The commitment required from the MEB Agency could be absorbed within the existing employee capacity. However, this is not the case for the reform of the new European pharmaceutical legislation that started in late 2023. To ensure that this reform produces a regulation that is workable for the Netherlands and the MEB Agency, substantial input is needed from the MEB Agency.

The replacement of the primary-process ICT system was started in 2022. The tender for the new system was scheduled for 2023, but this has been delayed. The current expectation is that this tender will take place in the first half of 2024. The associated costs will be covered from the funds allocated under the WaU programme.
In addition, activities will be undertaken in 2024 using WaU funds to strengthen the ICT security of the MEB Agency further.

In 2024, we will continue our work under the Information Management in Order (IoO) programme to make the MEB Agency compliant with the Woo. For this purpose, the Ministry of Health, Welfare and Sport has also made additional funds available.

From 2024 to 2026, the MEB Agency will contribute to the EU project IncreaseNet. IncreaseNet falls under the EU4health programme. IncreaseNET focuses on regulatory capacity building in the European medicinal products network. To carry out its activities, the MEB Agency receives a contribution from the European Commission and the Ministry of Health, Welfare and Sport.

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Due to retrospective adjustments to the MEB database, some figures from previous years in this edition of the annual report may differ from the figures as published in the annual reports of previous years.

Appendixes

Human medicinal products and vaccines

Table 1.1a Assigned rapporteurships and co-rapporteurships through the centralised procedure (CHMP)

Year	Co-rapporteurships	Rapporteurships
2018	5	18
2019	11	24
2020	10	19
2021	2	21
2022	5	17
2023	8	10

Table 1.1b Assigned rapporteurships and co-rapporteurships through the centralised procedure (CHMP) per country

Country	Number of rapporteurships and co-rapporteurships
Germany	24
Austria	21
Sweden	19
The Netherlands	18
Denmark	14
France	14
Poland	14
Republic of Ireland	13
Czech Republic	11
Finland	11
Portugal	8
Italy	7
Croatia	6
Slovakia	6
Belgium	5
Romania	5
Iceland	4
Latvia	4
Norway	4
Spain	4
Estonia	3
Hungary	3
Slovenia	3
Lithuania	1
Bulgaria	0
Cyprus	0
Greece	0

Luxembourg	0
Malta	0

Table 1.2a Assigned pharmacovigilance rapporteurships (PRAC)

Years	Other substances	New substances
2018	5	11
2019	12	19
2020	9	11
2021	5	17
2022	8	16
2023	3	11

Table 1.2b Assigned pharmacovigilance rapporteurships (PRAC) by country

Country	Number of rapporteurships
Germany	20
Sweden	16
The Netherlands	14
Spain	11
Denmark	10
Republic of Ireland	10
Belgium	8
France	6
Finland	5
Austria	3
Croatia	3
Italy	3
Lithuania	3
Czech Republic	2
Norway	2
Poland	2
Hungary	1
Latvia	1
Bulgaria	0
Cyprus	0
Estonia	0
Greece	0
Iceland	0
Luxembourg	0
Malta	0
Portugal	0
Romania	0
Slovakia	0
Slovakia	0

Table 1.3a RMS applications launched through the decentralised procedure (DCP) and mutual recognition procedure (MRP)

Years	MRP	DCP
2018	57	211
2019	60	235
2020	85	174
2021	93	162
2022	69	111
2023	56	180

Table 1.3b RMS applications initiated through the decentralised procedure (DCP) and mutual recognition procedure (MRP) per country

Country	MRP	DCP and MRP
Germany	48	297
The Netherlands	56	236
Sweden	35	165
Portugal	21	108
Denmark	23	106
Czech Republic	18	87
Hungary	8	70
Iceland	2	64
Republic of Ireland	12	50
Austria	10	40
Malta	6	39
Poland	10	37
Finland	7	32
Spain	8	29
Lithuania	4	25
Slovenia	2	22
Croatia	2	19
Slovakia	4	19
Estonia	7	18
Latvia	4	14
France	9	12
Norway	8	12
Italy	1	9
Cyprus	3	8
Belgium	3	5
Romania	1	3
Bulgaria	2	2
Greece	0	1
Luxembourg	0	0

Table 1.4 Applications submitted through the national procedure

Years	Applications submitted

2018	57
2019	67
2020	87
2021	59
2022	80
2023	63

Table 1.5 Parallel import applications submitted

Years	Applications submitted
2018	521
2019	375
2020	316
2021	486
2022	302
2023	224

Table 1.6a Number of registered marketing authorisations

Years	Registered marketing authorisations
2018	14,288
2019	14,288
2020	13,565
2021	13,452
2022	13,577
2023	13,774

Table 1.6b Number of withdrawals after registration

Years	Withdrawals
2018	1,209
2019	1,390
2020	1,649
2021	1,150
2022	859
2023	549

Table 1.7 Number of scientific opinions assigned through the SAWP

Years	Number of scientific opinions assigned
2018	130
2019	142
2020	140
2021	146
2022	140
2023	106

Table 1.8 Opened cases for national scientific opinions

Years	Scientific opinions	Tailored scientific opinions
2018	110	6
2019	115	14
2020	103	10
2021	95	6
2022	98	12
2023	105	9

Table 1.9 Number of Direct Healthcare Professional Communications (DHPCs)

Years	Number of DHPCs
2018	31
2019	29
2020	22
2021	26
2022	20
2023	14

Botanicals and novel foods

Table 2.1 Number of registered marketing authorisations for herbal medicinal products

Years	Based on a complete dossier	Based on traditional use
2018	52	53
2019	49	55
2020	43	55
2021	37	50
2022	37	48
2023	35	44

Table 2.2 Number of registered marketing authorisations for homeopathic medicinal products

Years	Number of registered marketing authorisations
2018	2,132
2019	2,130
2020	2,034
2021	2,013
2022	2,041
2023	2,044

Veterinary medicinal products

Table 3.1 Assigned centralised CVMP rapporteurships and co-rapporteurships

Years	Number of assigned CVMP rapporteurships and co-rapporteurships
2018	5
2019	4
2020	1
2021	16
2022	7
2023	1

Table 3.2 Assigned centralised MRL rapporteurships and co-rapporteurships

Years	Number of assigned MRL rapporteurships and co-rapporteurships
2018	3
2019	2
2020	2
2021	0
2022	0
2023	1

Table 3.3a RMS applications closed through the decentralised (DCP) and mutual recognition procedure (MRP)

Years	MRP	DCP
2018	2	14
2019	1	41
2020	0	40
2021	0	30
2022	0	28
2023	2	50

Table 3.3b RMS applications closed through the decentralised (DCP) and mutual recognition procedure (MRP) per country

Country	Number of MRPs and DCPs
The Netherlands	27
Republic of Ireland	18
France	17
Czech Republic	7
Spain	4
Hungary	2
Austria	1
Belgium	1
Estonia	1
Germany	1
Sweden	1
Denmark	0
Finland	0
Italy	0
Norway	0
Poland	0
Portugal	0
Slovakia	0
Slovenia	0

Table 3.4a Number of registered marketing authorisations for veterinary medicinal products

Years	Number of registered marketing authorisations
2018	2,292
2019	2,329
2020	2,382
2021	2,349
2022	2,279
2023	2,246

Table 3.4b Number of withdrawals of marketing authorisations after registration of veterinary medicinal products

Years	Number of withdrawals after registration
2018	108
2019	98
2020	60
2021	139
2022	143
2023	153

Governance and organisation

Table 4.1 Objection and appeal procedures

Years	Number of objection and appeal procedures
2018	34
2019	30
2020	30
2021	32
2022	30
2023	23

Table 4.2 Number of hearings and opinions

Years	Number of hearings and opinions
2018	23
2019	19
2020	26
2021	15
2022	24
2023	11

Table 4.3 Number of employees and full-time equivalents (FTEs)

Years	Employees	FTEs
2018	386	351
2019	378	341.6
2020	408	374
2021	421	387
2022	460	423.5
2023	511	474.7