CBG MEB

COLLEGE TER BEOORDELING VAN GENEESMIDDELEN

Regulating with the knowledge of tomorrow

Science Policy 2020 - 2024

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Medicines Evaluation Board

Contents

Foreword

The Medicines Evaluation Board has a number of clearly defined statutory tasks. These are assessing medicines, monitoring adverse reactions and risks and stimulating the proper use of medicines for humans and animals. All those tasks are based on a common foundation, namely science.

This Science Policy describes the strategic direction of our scientific focus in the period between 2020 and 2024 as we continue along the course plotted by our Strategic Business Plan (SBP) during the same period, in line with our core values of being scientific, vigilant and connected. Our aim is to improve the assessment and the usage and people's trust in medicines. After all, ultimately we do our work on behalf of patients.

Within the framework of this science policy we have adopted 8 main themes which we are going to focus on in the coming years. These are cross-dossier themes which are linked to developments in society, such as the replacement, reduction and refinement of animal tests, personalised medicine and the influence of big data on the assessment of medicines. Many of the themes are relevant for both the development of medicines for humans and for animals.

Although these 8 main themes define the course we are going to follow in the coming years, this does not mean we are prevented from exploring other avenues. We will continue to pay close attention to any developments which influence our work and public health together with our chain parties in the field of medicines and various other (academic) partners. In all of this we will not lose sight of the patient and the patient perspective will be taken into account whenever any research is started.

Finally, we would like to thank everyone who has contributed to the creation of this Science Policy, in particular all MEB employees, Board members, members of the Science Committee, members of the Advisory Board and the employees of the Ministry of Health, Welfare and Sport (VWS) who have shared their insights and knowledge with us on behalf of this Science Policy.

Ton de Boer
Chairman

Hugo Hurts
Board and CRD director/secretary

Summary

Science and scientific data form the foundation for our statutory tasks at the MEB and the scientific analysis of data is actually an important basis for our assessments of medicines. The process of assessing medicines often leads to research questions which are not restricted to a single dossier and instead affect the entire regulatory system. We look for answers to these questions by conducting scientific research in the domain of 'Regulatory Science'.

When doing so we apply two principles:

1. System improvement (including optimisation and deregulation).
2. Innovation which is of added value for the MEB's role and task (renewal).

Our aim is to continue to ensure the availability and accessibility of medicines for patients. We also want to make sure that our organisation is future-proof and we will continue to renew and improve our regulatory system, embed knowledge in our work, inspire employees and contribute to a strong (inter)national scientific and regulatory network.

Themes

In order to guide our scientific activities, the MEB has identified 8 themes in which we will invest in the coming years, in line with the MEB's Strategic Business Plan (SBP) 2020-2024:

1. **Replacement, reduction and refinement of animal tests (3Rs)**
2. **Advanced Therapy Medicinal Products (ATMPs)**
3. **Data-driven assessment**
4. **Personalised medicine & biomarkers**
5. **Medical devices**
6. **Generics**
7. **Medicines used better**
8. **Safety and effectiveness after authorisation**

Other developments

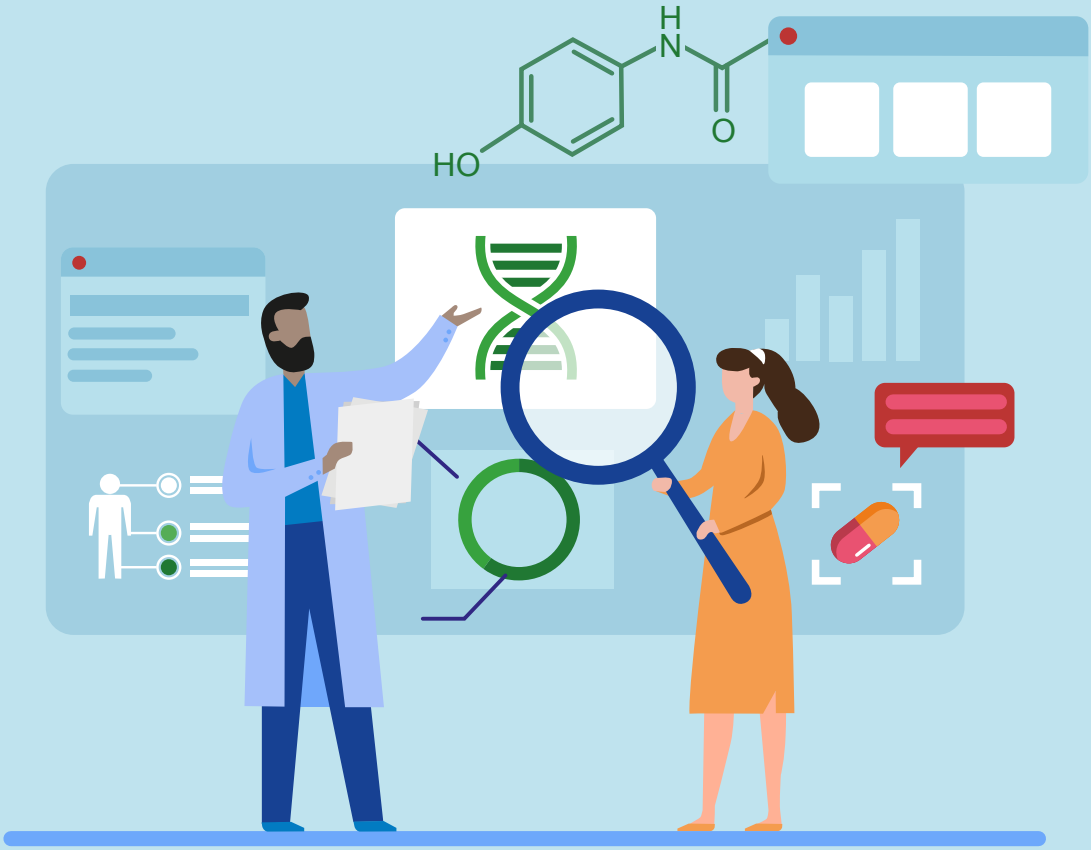
It is important to the MEB that it can adapt to current developments which influence our work and public health. The themes described are therefore the most important focus for the coming years, but do not entirely rule out any other studies. We as an organisation can anticipate change by conducting regular horizon scans and environmental analyses and by monitoring scientific research.

Developing and securing knowledge

In order to make optimal use of knowledge obtained from Regulatory Science, we want to invest in the development, safeguarding and sharing of knowledge both internally and within the network. We will do this by implementing research results in our work process wherever possible, but also through education, for both MEB employees and for external target groups.

Cooperation

Regulatory Science is a cross-border phenomenon and extends across the entire international regulatory system. That is why, when carrying out scientific activities, we frequently collaborate with academic groups, other scientific knowledge institutions and other authorities in our network (national medicines authorities and the European Medicines Agency). We are also a member of various public-private partnerships, such as the Regulatory Science Network Netherlands (RSNN) and Innovative Medicines Initiative (IMI) projects, in which patient representatives and pharmaceutical umbrella organisations participate. Thanks to this continuous cooperation with, and knowledge sharing and exchanges within our network, we are able to implement solutions which make the process of regulating medicines faster, more efficient and more flexible.



1 The MEB and science

The Medicines Evaluation Board (MEB) is responsible for the authorisation and monitoring of medicines on the market in the Netherlands. We assess the quality, efficacy and safety of medicines for both humans and animals. We also invest in improving information on medicines for care providers and patients. We do this in the interest of public health. Every day we work to increase people's trust in good medicines that are used better.

1.1 Scientific basis

Science and scientific data form the foundation for our statutory tasks at the MEB and the scientific analysis of data actually is the basis for our assessments of medicines. The knowledge accumulated during these assessments helps increase the expertise of our employees. During an application procedure our employees also have the possibility of consulting external experts about the latest scientific or technological developments. We fulfil a prominent role in various European scientific committees and working groups and part of our statutory task is also to provide scientific advice to companies and academic groups in the early phase of development of medicines. The development of scientific knowledge therefore takes place largely during the primary assessment process of medicines.

THE SCIENTIFIC ANALYSIS OF DATA IS THE BASIS FOR OUR ASSESSMENTS

At the same time that primary process generates cross-dossier research questions which affect the regulatory system of assessments of medicines as a whole. As an organisation we also have to find regulatory responses to new scientific developments. That is why we are reinforcing our scientific foundation by carrying out scientific research in the domain of '**Regulatory Science**'. Within this domain the MEB not only investigates issues which affect the assessment of the efficacy, risks and safety of medicines, but also issues relating to the regulatory system itself. We make sure science aligns with our core task. That is why we carry out scientific activities on the basis of two principles: 1) system improvement (including optimisation and deregulation) and 2) innovation which has added value for the MEB's role and task.

> **Regulatory Science** is an applied science which, via various scientific disciplines, assesses internal regulations and policy in relation to the assessment of the entire life cycle of medicines. New insights contribute to 'evidence based regulatory practice': It involves answering questions such as: are we doing things properly, do adjustments need to be made on the basis of new knowledge and are we prepared, based on our current knowledge and expertise, for change and innovation?' Regulatory Science is also aimed at the development and improvement of instruments, standards and working methods used to assess medicines in terms of efficacy, risks and quality and the improvement and innovation of the system as a whole.

1.2 Objective

The MEB's scientific activities serve several purposes:

- **To continue to ensure the availability and accessibility of medicines for patients** by having the latest scientific insights, innovations, tools and expertise for the high-quality assessment of medicines.
- **To innovate and improve our regulatory system** through continuous assessment of internal regulations and by influencing international guidelines and policy.
- **To make the organisation future-proof** by anticipating and contributing to new, innovative developments.
- **To anchor and secure knowledge in our work** by translating scientific insights and results into daily (assessment) practice.
- **To inspire and help (potential) employees develop** by enabling them to combine research, supervision or educational activities with their primary work.
- **To contribute to a strong (inter)national scientific and regulatory network** by combining our own expertise with the knowledge and expertise of academic groups and other knowledge institutes and by strengthening our partnerships.

In order to achieve this, we invest in our employees, science education and research, which is based on this long-term science policy. In this policy the MEB specifies the role and significance of science for the organisation, themes we invest in, how we implement scientific results and which resources we use. The policy provides frameworks to guide our work in the coming years. The practical details of this policy, including the way in which we are going to evaluate it, will be presented in the 'Science Implementation Plan.

> IN THIS POLICY THE MEB SPECIFIES THE ROLE AND SIGNIFICANCE OF SCIENCE FOR THE ORGANISATION

1.3 Creation

The science policy is in line with the Strategic Business Plan 2020-2024 (SBP), in terms of scientific developments. In addition, the MEB also conducted an internal consultation and an external study using the topics in the SBP as a starting point. The policy has been written against the backdrop of the national and international context in which the MEB operates. We have aligned the content of the policy with the developments and plans of, among others, the Ministry of Health, Welfare and Sport (VWS), the European Medicines Agency (EMA)[1], the Heads of Medicines Agencies (HMA)[2] and the International Collaboration of Medicines Regulatory Authorities (ICMRA). Investing in knowledge through Regulatory Science is prominently on the agenda of the EMA and the U.S. Food and Drug Administration (FDA), among other regulatory authorities. Our aim is to ensure that our efforts in the field of Regulatory Science benefit the international network we operate in.

1 Regulatory Science Strategy to 2025 and European medicines agencies network strategy to 2025
2 HMA Multi-Annual Work Plan

2 Themes

In order to give direction to our scientific activities, the MEB has identified 8 themes we are going to invest in during the coming years. The themes regularly interface or overlap with each other and relate to several domains of the life cycle of medicines (we make a distinction between the pre-authorisation, authorisation and post-authorisation phase).

The MEB (in collaboration with other regulatory authorities) has to find a regulatory response to the developments within those themes, of which different forms of treatment, a more personalised approach to our health and changing legislation and regulations are just a few examples. These developments force us as an organisation to carry out critical and continuous reviews of our own assessment system and make improvements. For each theme we clarify what we want to achieve in the coming years and what the connection is between science and the regulatory work within the domains.

2.1 Replacement, reduction and refinement of animal tests (3Rs)

The development of medicines goes hand-in-hand with animal research, both in the early phase of the development (before the medicines are tested on humans) and during the clinical phase. The MEB critically evaluates the added value of animal research in medicine development because current evidence suggests that data from animal studies cannot always be translated to humans. That is why we are contributing to research into the suitability of alternative models for efficacy and safety in medicine development, and why we are evaluating the need for animal studies in international guidelines. We are also working to identify the most efficient way of assessing the safety of new classes of medicines based on as few animal studies as possible (or with non-conventional studies). In that way animal testing will only be carried out if there is real added value and our aim is to create a future in which these tests are replaced as much as possible by alternative methods.

In the coming years we are going to be working with, among others, The European Partnership for Alternative Approaches to Animal Testing (EPAA) and the National Centre for the Replacement Refinement and Reduction or Animals in Research (NC3Rs) on an evaluation of the regulatory requirements for animal testing for monoclonal antibodies. The aim is to reduce the length of toxicity studies in test animals.

We are using the results of the 3Rs research in the scientific advice procedure when companies or academic groups ask questions about their development plan for a medicine and the use of animal studies in the process. Our research contributes greatly to a change in regulations at international level.

2.2 Advanced Therapy Medicinal Products (ATMPs)

In Europe, it has been ten years since work began on a separately defined group of innovative medicines, known as Advanced Therapy Medicinal Products (ATMPs). The MEB wants to remove unnecessary obstacles to the development of these products so that they become more readily available to patients for whom an ATMP therapy could result in substantial improvements in their clinical picture.

The process of developing these therapies is fundamentally different to the development of more regular medicines because the basis of the medicines consists of human genes, cells or tissue. The mechanisms of action of these medicines is also fundamentally different and sometimes involves treatment which consists of a single administration with long-term, possibly lifelong effects. That is why we are investing in knowledge and research about the treatments, the techniques used and the regulations. We are evaluating which requirements have been imposed on the development programmes of ATMPs, so that we can then take a critical look and decide whether guidelines have to be adapted. We are identifying the consequences of this type of treatment for the monitoring of the medicines on the market. We also take the latest scientific developments into account in the scientific advice we provide. All of this increases the consistency of our decisions, increases the quality of our advice and ensures that we can make a substantial contribution in the coming years to the international discussions about this topic, which will make it easier for patients to access this group of medicines.

2.3 Data-driven assessment

The scientific analysis of data forms the basis for our medicine assessments. Medicine dossiers contain a huge amount of data and the nature, sources and possibilities for applying this data are developing continuously.

Real world data & Big data

In the coming years we are going to identify the influence and consequences of the emergence of big data and real world data and the resulting opportunities for medicines authorisation and monitoring. Important questions in this context are, for example: Which data sources are of added value and (how) can other (sometimes new) forms of data be included when assessing the benefits and risks? Which analysis options must we, as an organisation, have at our disposal to be able to assess other data than that from the 'classical studies' and what demands does that place on our infrastructure and the competences of our employees? The MEB is going to perform additional scientific research into this in collaboration with other parties.

Patient reported outcomes and patient preferences

An example of current changes are, for example, the patient experiences which 'are captured' (patient reported outcomes, also referred to as PROs). These concern endpoints which the patients themselves assess and are based on the patient's perception of the symptoms of the disease and/or the effect of the related treatment. PROs can be used to obtain an additional insight from another perspective of the observed effect of the treatment by and for the patient. This in turn facilitates a more patient-oriented assessment of medicines. There are also differences between patients in how they value the importance of the effects of medicines. In this respect patient preference studies can generate insights which make the assessment of medicines more patient oriented. For that reason we are going to perform additional research which will, for example, establish what exact role PROs can play in the regulatory process compared to the more usual 'clinically relevant' outcomes in a randomised clinical study.

Data strategy

In order to structure the way we approach the various issues relating to data, the MEB will prepare a data strategy in which we specify what we want to achieve by using big data and real world data and how we will work to achieve that. We are also reflecting on the demands we impose on submitting real world data in the dossier of new medicines, bearing in mind the quality aspects of data, standards and data ownership. In the data strategy attention will also be paid to the 10 recommendations made by the Big Data Task Force of the EMA and HMA and we will decide on the role the MEB can additionally play in that context. We recognise the importance of data harmonisation and standardisation and, as an organisation, we are working actively to achieve this (for example by setting up the European Substance Registration System). We are also addressing research questions related to modelling, simulation and extrapolation.

On top of all this we are investigating the practicability and possibilities of analysis tools in the context of our assessments. We have noticed that other national agencies in Europe are setting up their own data centres. As an organisation we will decide which options we have in this regard and this will enable us, as an organisation, to stay future-proof and able to deal correctly with important data analyses which will improve the quality of our work.

2.4 Personalised medicine & biomarkers

The MEB intends to find a regulatory response to the development of personalised medicine for the authorisation of medicines for more specific groups of patients. In doing so a patient's unique individual characteristics will serve as a basis for choosing optimal individual therapy for the patient in question. Patient populations selected on the basis of a biomarker[3] may be small or consist of patients with various disorders which nevertheless share the same biomarker. This means that large-scale Randomized Controlled Trials are impossible in conjunction with these specific groups of patients. Innovative trial designs are needed to generate sufficient and relevant evidence of efficacy and safety. In 2019 the EMA approved the first medicine for a histology-independent indication. Up to now limited experience has been gained with these types of assessments and there are concerns that it may be impossible to obtain sufficient convincing clinical evidence for these types of indications. There is also a need for knowledge on new methodologies in order to determine what is appropriate when developing medicines for personalised medicine. The MEB thinks it is important to conduct more research on this which will focus primarily on the validation of biomarkers, alternatives in the medicine development (clinical study designs, statistics, outcome measures, patient selection and control groups), and the possible use of real world evidence. This way, we prepare our regulatory work for the possibilities and challenges of personalised (or precision) medicine, with the aim being for patients to benefit.

2.5 Medical devices

Medical devices and In-vitro Diagnostics are being used more frequently in a personalised approach to health, both individually and in combination with medicines. The category featuring a combination with medicines is having an impact on our organisation's work. In 2017 two European directives entered into force for medical devices and In-vitro Diagnostics. These are coming into effect in 2021 and 2022, respectively. The aim of the revised Medical Device Regulation (MDR) is to achieve greater consistency in the assessment of Medical devices in the EU in terms of product quality and patient safety, while the certification requirements for In-vitro Diagnostics are better aligned with the importance of the test when it comes to treating a patient and the consequences of misclassification.

The MDR is also the reason to further define the assessment framework for medicine device combinations. The MEB is participating in the EMA working group which is developing the relevant guidelines. At national level, the focus is on the intended use by the patient/professional, in other words research and policy development with regard to using the medical device in combination with the intended medicine.

Another major change compared to the current situation is that clinical evidence has to be provided for companion diagnostics (In-vitro Diagnostics which are linked to a medicine). With the new regulation a notified body is responsible for assessing companion diagnostics. However, because the benefit-risk balance of the medicine can depend on the companion diagnostic, close cooperation between the EMA, national agencies and the notified bodies is required. Among other things the MEB will carry out evaluation research into the points raised during discussions in recent years in centralised procedures and European scientific recommendations in relation to companion diagnostics. This research will be used for the regulatory guideline which is being written on the development-related challenges of personalised medicine with companion diagnostics following implementation of the new requirements in 2022. It is also important to investigate the extent to which various diagnostic tests for the same biomarker generate the same results, given that this can affect the process of weighing the benefits and risks of a medicine.

3 Biomarkers are biological markers which can indicate that someone has a disease, which can predict how serious a disease course will be, or which show whether a treatment is working or not. One example of this is PDL-1 protein expression for immunotherapy in the context of oncology.

2.6 Generics

More than 75% of the prescribed medicines issued by public pharmacies are generic medicines and are used by large numbers of patients. Research has shown that having to change medicines, as often occurs in the case of generics, has an effect on patients' trust[4]. That is why the MEB is conducting research into the interchangeability of generics to establish which differences are acceptable and which risk minimisation measures have to be taken in the event of differences. The MEB is also investigating how to deal with the assessment of generics for which no EU reference product has been registered. Our aim is to contribute to patients' trust in generic medicines.
The MEB was also commissioned by the Ministry of VWS to put together an overview of medicines for which changes are undesirable, for example because the incorrect changing of these products can lead to serious health issues. In connection with this list, we are drawing up scientific conditions which are to be discussed with patient organisations and umbrella organisations of physicians, pharmacists and healthcare insurers.

2.7 Medicines used better

The MEB's aim is to encourage the proper use of medicines by making the information on medicines provided by the MEB to care providers and patients (for example the package leaflet) more accessible and more understandable. We are also helping to tailor information on medicines to a certain target group, for example elderly patients. Information which is easier to understand and more accessible will help increase medication safety, reduce wastage and improve shared decision-making.
Scientific research on this theme relates to activities carried out throughout the organisation. We are using the research outcomes to draft and assess the package leaflets and other information on medicines, as well as to improve the accessibility of the MEB website with information on medicines; geneesmiddeleninformatiebank.nl. With a view to expanding on the developments in relation to this theme, the MEB initiated the Better Use Programme [Programma Goed Gebruik].

2.8 Safety and effectiveness after authorisation

An important part or our work is to continuously monitor those medicines that are already on the market. We monitor safety and take actions to minimise the risk during use and to promote the effectiveness of these measures. In the coming years we will focus our scientific activities on, amongst others, research into the effectiveness of risk communication (e.g. Direct Healthcare Professional Communications) and risk minimisation measures and the use of medicines during pregnancy. We will also focus on signal detection and its optimisation. We can do this by carrying out research into those non-serious adverse effects that have a major impact on a patient's quality of life, and into adverse effects in specific patient populations, such as children and the elderly. In addition to safety, we believe it is important to focus on the positive effects of a medicine and we want to make sure that, if there is robust evidence for another indication, this can result in changes in the product information. Registries play an important role in the proper collection of data in order to monitor effectiveness and safety after marketing authorisation. We contribute with our expertise to the 'Management of Registries' [Regie op Registers] feasibility study by the Dutch National Health Care Institute [Zorginstituut Nederland]. This study is aimed at creating conditions and frameworks for registries for both marketing authorisation and cost-effectiveness, which are in line with developments in our European network.

4 Nivel report 'Trust in medicines: questionnaire research involving the general public' [Vertrouwen in medicijnen: een vragenlijstonderzoek onder burgers], commissioned by the MEB

2.9 Other developments

The MEB wants to use Regulatory Science to adapt flexibly to other developments which have a major impact on our mission and affect public health, such as the COVID-19 pandemic. The MEB also thinks it is important to use the research questions generated by the organisation and our international regulatory network as a basis for its research programme. The themes described above are therefore intended to provide guidance and are not exhaustive.

> THE MEB WANTS TO USE REGULATORY SCIENCE TO ADAPT FLEXIBLY TO OTHER DEVELOPMENTS WHICH HAVE A MAJOR IMPACT ON OUR MISSION AND AFFECT PUBLIC HEALTH

Research questions that arise during assessments may justify further research, even if they do not directly fit in with the themes described above. After all we want our employees to be supplied with relevant, up-to-date scientific knowledge and we want to be able to perform our core task as well as we possibly can.

3 Implementation

In this chapter we describe how we are going to carry out the scientific activities related to the themes described above. Taking into account the long-term nature of this policy we will not invest in all the themes simultaneously with the same intensity. Choices will be made in the coming years on the basis of various factors, such as their urgency for public health, their impact on our core task and their relevance to our daily work.

3.1 Cooperation

The MEB is part of an international regulatory system. We carry out our core tasks, authorisation and monitoring, largely in collaboration with other national medicines authorities and the European Medicines Agency (EMA). Regulatory Science is also a cross-border phenomenon and that is why, when carrying out scientific activities, we frequently collaborate with academic groups, other scientific knowledge institutions and other authorities in our network. As an organisation we are, of course, also part of a national care chain, which can be affected by the research results. For that reason, we make sure that our own research agenda and those of national and international partners complement and reinforce each other wherever possible.

Through continuous cooperation with, and knowledge sharing and exchanges within, our network we are able to implement solutions which make the process of regulating medicines faster, more efficient and more flexible. Much of the regulation and decision-making take place at European level and that is

why it is essential to link up with (international) partners. Combining forces in the international network sometimes also generates opportunities to organise research on a larger scale. Our focus is on strengthening the knowledge and competence of the regulators, academia and pharmaceutical companies and on ensuring that research results benefit the entire network.

Cooperation with other organisations takes on a variety of forms. For example, the fact that several MEB employees who work at the MEB also work at a university makes it easier to exchange knowledge. When studying for a PhD, students have one foot in scientific research and the other in our assessment work, which leads to long-term partnerships with Dutch universities and university hospitals. Specific alignment and cooperation take place with national chain partners on a number of different themes. Examples include 'Better use' and 'Data-driven assessment' (for example registries), as well as 'Replacement, reduction and refinement of animal tests' and 'ATMPs'. In this way we can ensure that the outcomes of scientific research are relevant to our own regulatory system and to other parties in the care chain.

(INTER)NATIONAL COOPERATION IS ESSENTIAL

We also play a prominent role in cooperation with other national agencies in Europe and the European Medicines Agency (EMA) taking part in key scientific working groups and task forces, such as the EMA Big Data Steering Group and the EU Innovation Network. Furthermore, we collaborate on (inter)national research projects which are supported via ZonMW, the Innovation Medicines Initiative (IMI) and Horizon Europe (formerly known as Horizon2020). In addition, we are part of the STARS (Strengthening Training of Academia in Regulatory Sciences and supporting regulatory scientific advice) consortium, to which 18 national agencies and the EMA are affiliated[5]. The aim of this research project is to ensure that medicine development in academia is in better alignment with regulatory requirements and to strengthen regulatory knowledge by reaching clinical scientists in an academic setting during training[6]. In the future the MEB will also explore the role which we as an organisation can fulfil in ZonMw's Future Affordable and Sustainable Therapies (FAST) programme together with the other parties involved. We are going to retain and reinforce valuable partnerships like this in the coming years.

We are also making sure that research and knowledge sharing with chain partners does not interfere with our tasks and responsibilities. For that reason, the MEB, in principle, does not engage in direct, individual partnerships with pharmaceutical companies that perform scientific research in the context of medicine development. The MEB is, however, regularly involved in scientific research in which regulatory authorities, academic research groups and pharmaceutical companies work together (public-private partnerships). The difference is that these are scientific research projects in a non-competitive environment which are intended to help improve the regulatory system as a whole. In the context of these multi-stakeholder projects, the role of a regulatory authority like the MEB is important to ensure that the developments in the research project are in alignment with the regulatory requirements. This is also expressed in our participation in the Regulatory Science Network Netherlands (RSNN), which is a public-private partnership that offers a neutral platform in which we exchange important regulatory knowledge with all stakeholders and help setting the research agenda. In the context of regulatory

5 https://www.csa-stars.eu. The implementation of the STARS project has been supported by external funding from Horizon 2020

6 Leveraging future-proof collaborations with academic groups is an important aspect of the European medicines' agencies network strategy, of which the MEB is part.

scientific advice or projects which are similar in terms of content, the MEB can decide to commit to direct, individual cooperation with a pharmaceutical company. By doing so, the MEB aims to contribute to the development of regulatory requirements. The results will not only be of importance for the marketing authorisation application, but may also be used more generally in the context of developing regulatory requirements. This will benefit the public health and generate the greatest added value for the entire regulatory system.

3.2 Coordination

The MEB coordinates, and in many cases organises, its various scientific activities from a single department within the organisation, in order to create as much cohesion as possible. This relates both to scientific research and educational activities which are intended to improve the scientific basis or methodology of the primary assessment process.

Organising these activities from one central point generates a clear overview of the degree to which knowledge is being developed and secured regarding the above-mentioned themes and Regulatory Science as a whole. It also makes it easier to improve and adjust scientific initiatives and the links between them on a continuous basis. The research supply and demand can then be efficiently coordinated and cross-connections can be established between the various disciplines and departments. This does not mean, however, that MEB scientific initiatives are carried out by just one department. The tasks of executing and supervising scientific research and the organisation of various educational activities are carried out by various MEB departments. In addition, there is a close cooperation with various working groups including the MEB's internal Scientific Advice Working Group, the Multidisciplinary Working Group, the Knowledge Sharing Working Group, the Learning and Development Steering Group and the Methodology Working Group to ensure optimal cohesion between scientific research and securing knowledge.

Another major benefit of this centring of scientific activities at one location within the organisation is that it creates a clear point of contact for the outside world. This, in turn, increases the connection and cohesion with external scientific initiatives and partners and strengthens our position in our international network.

3.3 Horizon scanning

As an organisation the MEB proactively uses the horizon scanning technique and frequently carries out environmental analyses to anticipate changes in the world of medicine development and regulation[7]. We do this together with other medicines agencies. The outcomes of these scans and analyses help to guide the MEB's scientific activities and contribute to the management of the research agendas of important organisations and networks around us. Another benefit is that research then links up correctly with regulatory requirements, thereby supporting the rapid accessibility of medicines.

Another way in which we use the horizon scanning is by monitoring scientific research which the MEB does not actively contribute to. There are various academic groups involved in Regulatory Science that publish in peer-reviewed journals of which the study results may be relevant to our assessment work. We make sure that these study results are available to our employees and can be applied in our daily work.

7 This horizon scanning should not be confused with the Medicines Horizon Scan [Horizonscan Geneesmiddelen] of the Dutch National Health Care Institute.

3.4 Research

Within the context of the previously formulated themes there is a wide diversity of research questions, which can also have different origins. Recurring issues or dilemmas which come to light during the primary assessment process when assessing applications or when drafting scientific advices can also generate research questions. Research questions or research proposals can also be submitted by external parties, such as universities or large consortia. The MEB decides which type of research is suitable to answer each research question. This depends on the topic, the question, the scope of the research question, the urgency of the response, the budget and the contribution the MEB is asked to make. The need and necessity of the research for our work is also taken into account when deciding whether to accept the research proposals.
We make a distinction between a wide range of types of scientific research projects, such as a multi-year PhD project, research by an internal employee or an (inter)national research project. Some research questions can be answered by a student during a scientific internship. The research projects will largely produce one or more of the following results: an increase in scientific knowledge, a system improvement, or the development of a new assessment instrument. We reflect in advance on the possible impact of these results on the organisation and our system.

Evaluation study

We will invest more in evaluation research and 'outcome measurements' after completing the scientific research in order to assess whether the current regulations and work process are correct and whether the results contribute sufficiently to our statutory tasks. We also pay a lot of attention to the 'regulatory impact of scientific output'.

Participation by patients

The MEB likes to involve patient representatives in its work and the same applies to the scientific research we perform. Active involvement of patients in scientific research performed by the MEB has the aim to optimise the quality of the research and extent to which the outcomes can be implemented. Each project proposal should include a suitable approach which focuses on an assessment of relevance and feasibility from the patients' perspective. How patients or their representatives are involved may vary between different research projects.

Science Committee

The Board appointed the Science Committee to monitor scientific activities and their cohesion.
The Committee consists of representatives from the (Young) MEB and employees from various disciplines with close links to research. The Committee's task is to advise on research-related activities which take place within the MEB, to decide on participation in research projects of various sizes and their financing, and to coordinate and monitor the research which the MEB participates in. The Science Committee therefore has an important role in implementing this policy.

The Science Committee uses an assessment framework to determine which research proposals can be approved. Various elements of the study design are assessed of submitted research proposals, such as consistency, feasibility and practicability, as well as the implementation proposal. In order to assess the action plan in relation to patient participation, the Committee collaborates with the board member whose work focuses specifically on the patient perspective. In addition, the relevance of the research question for the MEB is also taken into account.

3.5 Developing and securing knowledge

Wherever possible the MEB wants to use the Regulatory Science results in the regulatory process and maintain the knowledge of relevant scientific developments at a high level for its employees. In addition to increasing knowledge and improving assessments, this also provides inspiration and a fresh perspective on our work. That is why we are investing not only in scientific research but also in developing and securing knowledge in both our own organisation and our (inter)national network.

> WHEREVER POSSIBLE THE MEB WANTS TO USE THE REGULATORY SCIENCE RESULTS IN THE REGULATORY PROCESS

Implementation of research results

In order to ensure that the research results are actually incorporated into the primary assessment process, we devote a great deal of attention to the implementation plan of the research proposal. We also make sure that the relevant disciplines, working groups and experts are involved from the beginning and we keep a constant eye on the integration into the organisation. Specifically, this means that the research proposal is accompanied by a description of how the outcomes of the research are to be communicated to the relevant stakeholders within the MEB and elsewhere and what is necessary to embed the results further in our daily work. In this way we can ensure that the results are eventually secured within the organisation, for example because they lead to a change in policy.

Education at the MEB

In the context of scientific knowledge development, the MEB uses education as the connecting link between scientific research and the primary assessment process (and vice versa). Scientific education is aimed at collective knowledge development, by which we mean that the content is relevant for at least one or more departments within the organisation. On one hand education[8] can be enhanced by results from scientific research and, on the other hand, also by important knowledge and expertise which employees have gained during the assessment process itself. Education contributes to the implementation of the research results, knowledge development based on the themes in this policy and new developments, and provides inspiration.

For example, we organise theme-based meetings for our employees several times a year at which both internal employees and external experts are invited to present. We also organise regular meetings which are open to all employees, during which students and PhD students can present their research results. In addition to this we make sure that we apply the relevant knowledge and expertise of our partners internally and share relevant research results of academic research groups within our organisation so that this knowledge can be used in the assessments.

Scientific research can also lead to changes in our daily work which then require our employees to have different or new competencies and skills.

On top of this, questions may be raised from within the organisation which relate to compentencies, for example, questions about the supervision of (PhD) students. Educational matters like these may be beyond the scope of the science policy and are coordinated and developed in close cooperation with the Learning and Development Steering Group [Regiegroep Leren & Ontwikkelen] and the HRM&O department in order to guarantee the right level of cohesion in the total education offered at the MEB.

Education by the MEB

We use the MEB's internal knowledge to strengthen the knowledge of regulatory science and medicines in our (inter)national network. We do this for example by collaborating on a curriculum for clinical pharmacologists and by contributing to EUPATI-NL, a training programme for patient representatives. Through education we also help train physicians, pharmacists and other care providers in the field of medicines regulation and the use of the regulatory product information of medicines. We also provide specific training to academic groups on the regulatory requirements for medicines development and we participate in and organise various (international) conferences.

Publication policy

Scientific research regularly results in one or more publications which are intended to make the research results publically available. The MEB has drawn up a publication policy for this purpose and we perform an internal assessment of the use of the MEB affiliation. This helps ensure that contributions by MEB employees are of a high quality.

8 At the MEB education and training is provided in various fields, such as content knowledge, skills and conduct.

4 Financing

The MEB finds it important to have suitable financing for all its work; the same applies to our scientific activities. That is why we continually focus on finding ways to cover the costs of scientific activities. The research budget is a structural element of the MEB's annual budget and the scientific activities are explicitly included in the organisation's annual plan. Some of our research projects are carried out on the basis of external funding received from funding organisations such as ZonMW, IMI and Horizon Europe. On top of that we actively look for other ways of financing research activities

The MEB chooses to spend the majority of the research budget - either as direct funding, or as in-kind contributions - on research questions which are in line with the themes referred to in this science policy. When doing so we also make sure funding is available for research which falls outside these themes, but this represents a much smaller portion of the budget as a whole. We are mainly going to finance applied research, and to lesser extent fundamental research.

FOR EACH RESEARCH PROJECT WE ASSESS THE CONTRIBUTION REQUIRED AND THE CONTRIBUTION WE CAN PROVIDE

For each research project we assess the contribution required and the contribution we can provide. In the case of PhDs or internships, supervision is provided, in any event, by MEB employees and we also make frequent financial contributions by paying the salary of the PhD student or an internship allowance. In the case of (inter)national research projects, the contributions by the MEB can be diverse and take the form of, for example, a financial contribution, participation in the research project itself, or in a working group, advisory group or steering committee. The MEB may also get involved in the grant application phase of a research project, as long as this does not compromise its independent position. The required effort and financing are taken into account when deciding whether participation in a research project is possible.

Abbreviations and definitions

Afkorting	Verklaring
ATMP	Advanced Therapy Medicinal Product
MEB	Medicines Evaluation Board [College ter Beoordeling Geneesmiddelen]
EMA	European Medicines Agency
EPAA	The European Partnership for Alternative Approaches to Animal Testing
EUPATI-NL	Training course for patient representatives
FAST	Future Affordable and Sustainable Therapies
FDA	U.S. Food and Drug Administration
HMA	Heads of Medicines Agency
ICMRA	International Collaboration of Medicines Regulatory Authorities
IMI	Innovative Medicines Initiative
MDR	Medical Device Regulation
NC3Rs	National Centre for the Replacement Refinement and Reduction of Animals in Research
RSNN	Regulatory Science Network Netherlands
SBP	Strategic Business Plan 2020 - 2024
STARS	Strengthening Training of Academia in Regulatory Sciences and supporting regulatory scientific advice
VWS	Ministry of Health, Welfare and Sport
ZonMw	The Netherlands Organisation for Health Research and Development is an organisation for health research and innovation in the care sector

2020

Anyone who uses medicines should be able to trust them. That is what the Medicines Evaluation Board (MEB) is working on each and every day, in the Netherlands and in Europe.
Good medicines used better.

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