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Content

A network for health in Europe

The European system for the authorisation and supervision of medicinal products is unique worldwide. Thousands of experts work together in a network of around 50 national regulatory authorities and the European Medicines Agency. Scientific and technological developments place new demands on cooperation.

The pandemic has brought the topic of medicines regulation into the public eye to an extent that was hardly imaginable in the past. Has the (collaborative) work of the EMA and the national regulatory authorities changed as a result?

Prof. Dr. Karl Broich
President of the Federal Institute for Drugs and Medical Devices (BfArM)

Karl Broich:
We see this dynamic very positively and as an opportunity for patients in the EU. The pandemic has enormously accelerated certain developments in the health-care sector - let's just take the example of digitalisation. At the same time, it has become clear how much cooperation in the EU network matters, for example, in that we can access shared data. Ultimately, new forms of collaboration have emerged that benefit everyone – such as the creation of a digital EU database around supply shortages, which facilitates exchange between the EMA and the national competent authorities. Our common goal is therefore to use this momentum to translate our insights into sustainable systems and processes.

Emer Cooke
Executive Director of the European Medicines Agency (EMA)

Emer Cooke:
Our regulatory network is a collaboration model, so whether we are in a crisis or not, the collaboration continues. During the pandemic, our work with EU partners and national regulatory authorities was astounding: we collaborated, adapted, and accelerated our processes, both proactively and when we were required to do so. The key is to make sure that the spirit and energy behind that collaborative effort across the EU doesn't get lost as our work returns to 'normal'. Medicines regulation is no less important now and new challenges are always emerging such as medicines shortages, antimicrobial resistance and more, which require the same collaborative effort. We know that we can achieve much more when we work effectively together.

The regulation on EMA's extended mandate became applicable in March 2022. The EMA has been given more powers and performs more coordinating tasks than before. How does this affect the European medicines regulatory network? Are decision-making competencies shifting here?

Karl Broich:
The extended mandate has not changed the basic system for regulating medicines in Europe. In it, the EMA, just like the BfArM, is a member of the network of the heads of the national competent authorities, abbreviated as HMA. In it, we jointly use our resources and expertise to ensure good healthcare in Europe. As society changes and evolves, we must also evolve to fulfil this mission in the best possible way. For example, the fact that the EMA will play a coordinating role in defined crisis situations will benefit everyone. Ultimately, after all, the national experts work in the EMA's committees - including those that come into being as part of the extended mandate. So this is not about taking competencies away from national authorities. Rather, we are talking about how we can organize our work even better in the future, how we can coordinate optimally in times of crisis. In this way, the expanded mandate has a tangible effect on rapid and efficient exchange.

Emer Cooke:
The pandemic showed the best side of our network in action: we pulled together all our expertise, adapted our processes and collaborated with our EU partners to roll out the largest immunisation program in European history. This couldn't be done without a central coordinating body. The extended mandate recognises the way EMA adapted to the pandemic and took on new responsibilities such as the handling of medicines shortages and crisis coordination. It doesn't remove decision-making powers at the national level, but enhances our ability as a network to collaborate and coordinate our efforts during ongoing crises and ensure we, collectively, are better prepared and ready for future crises.

From preclinical research to pharmacovigilance, AI tools are playing an increasingly important role in regulatory business. For example, AI can be applied to establish a link between individual patient characteristics and the efficacy of a drug. On this basis, the optimal subject group for clinical trials could then be determined. Let's look into the future: will the expertise of the EMA and national regulatory authorities no longer be needed at some point?

Emer Cooke:
AI has a broad spectrum of applications and the potential to impact EMA's internal processes and the entire product lifecycle. As it plays a bigger role in the development of medicines, we anticipate changes to the content of the marketing authorisation applications of the medicines we approve, but also opportunities to improve the efficiency of our procedures and some of the associated administrative work. As regulators, our role is to ensure that the benefits of AI outweigh the risks and continuing to make sure we put patient's health first. As we continue to see more AI usage in medicines development, patients will look to us for assurances. We will always need our national experts to help guide the uptake of AI to ensure safety is embedded as the technology evolves, and the benefits of AI are clear to everyone.

Karl Broich:
There are particular challenges around the use of AI. We are talking about the development of medicines and ultimately patient safety. The processes are characterized by a high degree of dynamism. Accordingly, we as national regulatory authorities are also constantly adapting our instruments and approaches. The BfArM is in dialogue with the relevant players, and we clearly see ourselves as a driver at the EU level. Of course, cooperation with the EMA is crucial. At the end of the day, we all have a common goal and want to achieve the best result for the care of the EU population. In the future, this will only be possible with the input of all national experts.

What exactly does this input consist of?

Karl Broich:
The use of AI in drug development is something new for all of us and brings with it a corresponding complexity. In order to act optimally at the EU level, early interaction with the national regulatory authorities and the EMA is an important building block. For example, in the "HMA-EMA joint Big Data Steering Group", set up by the HMA and EMA. It advises on priority setting and action planning. The aim is to increase the benefits of data and AI in regulation - from data quality and study methods to evaluation and decision-making.

Emer Cooke:
EMA is working with our partners in the EU, and internationally, to bring the full potential of AI tools to benefit all patients in the EU. Our national experts are central to this effort. We are working closely together as a network – using our full expertise – to make the most out of the opportunities it brings. Rather than waiting to see how AI disrupts our work; we are embracing the opportunities that AI can bring to our work and processes, and ultimately, to the lives of patients in the EU, while ensuring appropriate guardrails are in place. It is not a question of applying AI, but further developing AI and AI-specific capabilities across our whole network.

How will the proposal for the new EU pharma legislation impact our regulatory work in the future?

Emer Cooke:
Our goal as regulators is to ensure patients have access to safe and effective medicines. The revision of the EU pharmaceutical legislation is a unique opportunity to reshape medicines regulation in the EU. It will help enable us to rationalise the use of the limited resources in the network and to deal more effectively with complex regulatory processes as a basis for a future-proofed system. What the European Commission has put forward is an EU regulatory framework that is fit for innovative medicines, promotes greater access to medicines for patients, and addresses the major public health challenges of the future.

Karl Broich:
Our current pharma legislation is not fit for purpose for the new challenges. So I fully agree with Mrs. Cooke that we must reshape medicines legislation to address adequately new approaches, new methods, and the use of big data and AI in all stages of drug development and surveillance to make the best out of this for patients. Working together on this will provide us with a competitive regulatory framework compared to other regions. It should also increase availability, access and affordability of medicinal products as well as fostering diversification of production and reducing risk of shortages – all in the interest of patients. So I can reassure you, we recognise the need for change and our network is eager to change to fulfil our mission even better – the new legislation should set the framework for this.

We are experiencing a previously unknown dynamic in the network

The European Medicines Regulatory Network is a unique model globally serving more than 500 million people in Europe and with access to thousands of experts. The network is made up of national competent authorities, the Heads of Medicines Agencies (HMA), who work together with the European Medicines Agency (EMA). Future focus will be on the acceleration of licensing processes – including making use of artificial intelligence.

The network of the heads of the regulatory authorities responsible for the regulation of medicinal products for human and veterinary use in the European Economic Area (abbreviated as HMA), was founded in 1995. The HMA concerns itself with important strategic questions, provides consistency within the EU, and discusses tried-and-tested processes. The work is shaped by a common vision: quick access to secure and effective medicines for the people of the EU.

The HMA works in and with the European Medicines Agency (EMA) and is able to access resources and expertise from all over Europe. This expertise is introduced into the EMA committees, which concerns itself with the evaluation of new drugs or the monitoring thereof. This ensures that the regulation of medicines meets the highest scientific standards.

"Our mode of operation and the regulatory environment has changed a lot over the years. We are experiencing a dynamism in the network which we have previously never experienced," says **Prof. Dr. Karl Broich**. He is **President of the Federal Institute for Drugs and Medical Devices (BfArM), member of the HMA and chair of its management group (HMA-MG) since 2019**. "Digitalisation has become much more important, for example, because of the coronavirus pandemic. We experienced how in Europe it's so important to work together and also be able to access common data and networks." Society continues to develop,

and this also applies to the HMA, says Broich: "In mutual lessons-learned workshops, we looked in depth at the question of how the network should be set up and changed in order to be future-proof. The necessary competences and resources need to be built up to meet the ever more complex products and technologies." It's also clear that the regulatory processes should be accelerated and simplified wherever possible without compromising the quality.

This is also where artificial intelligence (AI) comes into play. **PhD Björn Eriksson, Director General of the Swedish Medical Products Agency (MPA)**, is certain: "Artificial intelligence will change a large part of the environment in which we work and it will also change healthcare and the development of new treatments." Eriksson has been in the position of Vice Chair of the HMA-MG since 2023.

He advocates for the European regulatory networks playing a strong role in the application of AI: "Europe will be measured against other regulatory authorities around the globe with regard to agility and speed. We need to offer incentives and position ourselves appropriately to present the EU as an attractive region for medical innovations."

The Swedish MPA already started working with AI in 2020. At the same time, the application of AI in medical technology is advancing, for example, in diagnostic disciplines such as radiology. "The development is happening very rapidly, and we need complex systems and qualified personnel to understand the opportunities and risks of AI," Eriksson stresses. "This requires expertise across sectors, so not just pure AI expertise. It is also about training our own people accordingly."

Expanding our pool of experts is a matter which the HMA is actively pushing ahead with. The HMA and EMA therefore started a pilot project in May 2023, which is aimed at oncologists. They are provided with regulatory fundamentals in an inhouse created program so that they are able to incorporate their knowledge in a very targeted way into the evaluation of medicines. A project which, in a similar form, is conceivable as an AI application.

"In many areas of our work, the chasm between developers and users is a major challenge," explains Eriksson. "As the HMA, we want to contribute to the network in order to overcome this divide. Especially when it comes to innovative treatments that should be made available quickly."
The potential for the application of artificial intelligence in medicines regulation is major and the time is right: "AI has moved forward in public discussion and people are starting to see concrete examples of its application in everyday life."

In the evaluation of AI, particular focus is placed on the analysis of large quantities of data. Development has gained significant dynamism, particularly in data analysis. >

The fundamentals of such analyses are the standardisation of data. It is the prerequisite for ensuring that these can also be used uniformly and intelligently across the EU. In collaboration with the EMA, the HMA therefore set up the database "Data Analysis and Real World Interrogation Network" (DARWIN EU), which collects "real-world data" (RWD). This does not stem from clinical studies, but from everyday medical care and is gathered, for example, by health insurers or care givers. This data is therefore becoming increasingly important for regulatory decision-making. The evidence generated from this can be relevant for evaluating the efficacy of a drug as well as for the phases before and after licensing. DARWIN EU generates an entire network consisting of healthcare data sources. The aim is to be able to carry out scientific analyses of regulatory questions securely and in line with data protection.

"The research network also initiates studies to collect findings using RWD. We will use this to further improve data analysis in the

"Artificial intelligence will change a large part of the environment in which we work, and it will also change healthcare and the development of new treatments."

**PhD Björn Eriksson,
Director General of the Swedish
Medical Products Agency**

evaluation of drugs," explains Prof. Broich, who is also Co-Chair of the DARWIN EU Advisory Board. "The application of new technologies and the findings gained from Big Data will be a benefit for public health, by accelerating the development of drugs and enabling earlier access to new treatments."

The HMA network is aware of the need to change – furthermore, it is committed to changing itself so that it can better meet its mission: to create added value for all of our interest groups, in particular patients in Europe. •

"The application of new technologies and the findings gained from Big Data will be a benefit for public health, by accelerating the development of drugs and enabling earlier access to new treatments."

Prof. Dr. Karl Broich,
Co-Chair of the DARWIN EU Advisory Board

Digitalisation

We are providing impetus and paving the way for innovation

Digitalisation is accelerating changes to society and enabling innovation in many areas. In the healthcare sector in particular, for the health of the people, it is important to enable and promote these innovations. Dr. Wiebke Löbker is head of the Innovation Office and explains what the BfArM is doing about this.

"We are always open to discussions with researchers and developers," says Wiebke Löbker and, with this, explains the special spirit in the BfArM's Innovation Office. With the drive in development, start-ups and research facilities should also quickly master licensing and bringing to market. To achieve this, it's important to involve those responsible in the discussions as early as possible. Among other things, the Innovation Office therefore offers "kick-off meetings" in the early phases of drug and medical device development, in which the further route forward is discussed and best planned.

"Our goal is to seize all opportunities which can improve the healthcare of patients," explains Löbker. As a regulatory authority, the BfArM must of course communicate and observe the statutory provisions. "We don't just provide information about the regulatory hurdles, but support our partners, tackle the hurdles together and provide guidance on the right way forward so that safe and effective innovations get to the patients quickly," says Löbker. What is also important for this is for developers to be familiar with and utilise the advisory and support opportunities. "We therefore actively approach

researchers and incubators and don't just wait until questions come our way. We are always delighted to receive new contacts and having our finger on the pulse of the latest ideas in healthcare," says Löbker. The employees at the Innovation Office are on the go with a wide spectrum of topics and are therefore able to provide wide-ranging support. Not only are they open to ideas, sometimes they are even the driving force behind them.

EU Innovation Network

In order to promote the innovations in the best way, the Innovation Office also cooperates with the other national authorities in a Europe-wide network. The EU Innovation Network (EU-IN) was launched in 2015 to strengthen the cooperation between the National Competent Authorities (NCAs) and the European Medicines Agency (EMA) in regulatory issues with regard to new therapies and technologies. The aim of the EU Innovation Network is to improve the currently available regulatory support for drug developers at a national and EU level, and to make it more attractive to innovators. Gaps in early regulatory support need to be closed, a platform should be offered for exchanging tried-and-tested procedures, and cooperation between innovators requires reinforcement. As a spin-off of the EU-IN network, the STARS Consortium (Strengthening Training of Academia in Regulatory Science) was founded in 2019, which looks into precisely these gaps and challenges and works on making improvement proposals.

STARS for researchers

Together with her innovation team, Löbker headed the STARS project. The project, designed over three years, for the first time brought delegates from national competent authorities in 18 EU members states, including the EMA, as well as other players in the licensing of drugs, together around one table. "It was about bringing the academic and regulatory world together." The aims were to analyse the knowledge and interests of academic research, to improve the advisory offerings of the authorities, and to work through targeted training programmes for the scientists. The now published paper – STARS Common Strategy – contains 21 concrete proposals and successful examples for already existing support offerings from Member States. For example, recommendations are being made to already offer researchers training in the fundamentals of drug licensing at the start of their careers, to establish networking opportunities and better information offers as well as to already take into account licensing-related aspects during the funding announcements and evaluation procedures. "With this project, as a network, we have come a good step closer in our aim of making the cooperation and support for researchers even more conspicuous."

Weak signals on the horizon

Innovations require exchange with as many stakeholders as possible, and an openness for other ways of thinking and new ideas. Not only does the BfArM invite all researchers to make contact with the Innovation Office as early as possible, it also takes on the job of searching itself: "Horizon Scanning" is the process which identifies "Weak Signals" for emerging trends and evaluates the impact they could have on our tasks and work in the BfArM," says the Innovation Office, explaining the process. The employees from the Innovation Office are themselves actively involved with the "Horizon Scanning" method. They aim to identify topics that are not yet being widely discussed, >

and looking as far into the future as possible. “We are in contact with many drivers of innovation and we perform research to identify trends and to trigger necessary change in the BfArM for this so that we, as the developers of tomorrow, can point others in the right direction,” explains Löbker. Of course, the employees of the Innovation Office also benefit from their contact with start-ups and researchers. “Healthy ageing” is currently one of the expected trends: “The population is ageing, so this will be a common topic, whether in the digital field or in the prevention of Alzheimer‘s,” explains Löbker. When topics are identified, the BfArM prepares itself for this, for example, by looking for experts among the employees or adding to them. Changes in the BfArM itself are therefore also an important building block for innovation.

Guarantee for ideal healthcare

“In a continuously and increasingly fast changing environment, we, the BfArM, want to identify challenges at an early stage and convert them into opportunities by actively approaching changes and managing them successfully,” is the explanation of change and project management, which forms a further pillar in the department. The focus is on sustainable and long-term change, which is relevant for achieving the goals. This extends from process change through to culture and communication aspects. A trigger for the change includes digitalisation and artificial intelligence, which are incorporated into various BfArM projects. The required changes are strategically designed and an extensive catalogue of measures benefits the BfArM vision alongside the ongoing activities: The BfArM is a guarantor for ideal healthcare for all people in Germany and the rest of Europe.

Frontrunner in healthcare

The pressure of the pandemic also accelerated processes at BfArM to protect the health of citizens. The Innovation Office is now drawing findings from this for the BfArM, and is analysing which changes can also be transferred into everyday situations to ensure that it is also well set up for the continuing dynamic environment in the future. “To do this, we are abandoning the silo mentality, working more and more cross-functionally and closely together, promoting collaboration and looking to see where we can exploit synergies,” explains Löbker. Löbker and her team are designing and accompany change projects for continuous ongoing development so that the BfArM continues to be the “frontrunner in healthcare provision in an inspiring working environment.” The work of the BfArM thus allows innovations to flourish – or as Löbker summarises: “We have a mindset which is open to innovation and we understand change as an opportunity for our future configuration.” •

“We have a mindset which is open to innovation and we understand change as an opportunity for our future configuration.”

Dr. Wiebke Löbker,
Head of the Innovation Office/
Change Management Office

Dr. Wiebke Löbker

Studied pharmacy. From 2009 to 2011, she was scientific officer at the Institute for Pharmacology and Toxicology at the Free University of Berlin. From 2011 to 2016, she was a consultant and team coordinator in the “Medicinal products” department of the Federal Joint Committee with a focus on early benefit assessment. Since 2016, she has been working as head of the Innovation Office/Change Management Office at the BfArM, as well as personal assistant to the President.

Cooperation

Working together for the best licensing process

Regulatory expertise on the one hand, and academic, clinical expertise on the other: if this expertise is brought together into a licensing process for new drugs, it will benefit people suffering from diseases. In a pilot project, scientists in clinical oncology now have the opportunity to get involved in drug evaluation. The BfArM is participating as a driving force at many points along the way.

If someone wants to get a drug licensed in the EU, they have to make an application to the European Medicines Agency (EMA). The documents are then scientifically evaluated there in the Committee for Medicinal Products for Human Use (CHMP).

The committee brings together around 60 experts. They largely come from the national competent authorities, which are connected via the network of Heads of Medicines Agencies (HMA).

The Member States work through the assessment of the application in various groups to prepare their decisions. To do this, data and documents from the applicant are screened in the national licensing bodies and carefully evaluated. Recommendations for or against the licensing of a drug are then fleshed out and ultimately presented to the committee members for discussion. Finally, the official recommendation of CHMP is given, while the formal license is issued by the EU Commission.

Particular challenges

The Chair of CHMP is PD Dr. Harald Enzmann, head of the "EU and International" office at the BfArM. He has been a member of the multinational committee for 15 years and knows all about the meaning of scientific expertise in the assessment of licensing applications. "Experts with specialist knowledge or clinical experience are often consulted during assessment to enrich the scientific discussion," reports Enzmann. "The scope ranges from specific questions regarding potential applications in clinical practice to the latest trial."

This process has particular challenges. One example is oncological disease patterns in which access to innovative drugs improves the chances of a cure or can prolong life. This also applies to giving patients speedy access to these treatments. For this, knowledge of new scientific approaches as they exist in academic-clinical research is important. The same also applies for the anomalies in the provision of specific diseases. "This knowledge should flow into our application assessments," says the CHMP chair.

STARS

Linking the regulatory work with clinical and scientific research is an important matter for the players at national and European level. The EU financed initiative "STARS – Strengthening Training of Academia in Regulatory Science" was thus launched. It aimed to strengthen regulatory knowledge in the academic research environment and make the clinical research more usable for the healthcare systems. The BfArM took part in this as one of the coordinating project partners. National authorities from a total of 18 European countries worked together on this project. They are now working on the implementation of strategies and experience from STARS.

The BfArM is playing an important role in several places at once, with the aim of getting these kinds of initiatives and projects off the ground across Europe. The BfArM president, Prof. Dr. Karl Broich, recognises the topic from the point of view of the BfArM, as the largest national approval body in the EU, and also in his role as chair of the HMA: "New scientific approaches for innovative medicines are frequently conceived in academic-clinical research," explains Prof. Broich. "As the HMA, we see a demand in many EU member states for promoting dialogue between academic-clinical research and national medicines authorities. It involves speaking together about regulatory aspects and, at the same time, closing any >

Heads of Medicines Agencies

The Heads of Medicines Agencies (HMA) is a network of the heads of the national competent authorities for human and veterinary medicines in the European economic area. The HMA works in the network for European medicines licensing with the European Medicines Agency and the European Commission. It is a one-of-a-kind model for cooperation and work sharing in regulatory matters, at both statutory and voluntary levels.

The HMA is coordinated and headed by the Management Group and supported by various working groups – responsible for various areas – and the permanent secretariat. The president of the BfArM, Prof. Karl Broich, is a member and current chair of the HMA Management Group. Furthermore, numerous experts from the BfArM work in the HMA working groups.

https://www.hma.eu/about-hma.html

gaps in information in the development of medicines." Together with the EMA, we are searching for pathways and potentials which can be exploited. This resulted in the idea of systematically approaching scientists in clinical oncology from across the EU and to bring them on board for this cooperation.

Pilot project oncology

Against this backdrop, the HMA and EMA therefore started a pilot project in May of 2023, which is aimed at oncologists. It will be introduced over a time scale of twelve months. The focus lies on scientific mentoring and assessment of the licensing of human medicines. The regulatory competence is to be reinforced by academic researchers, among other things by way of targeted training programmes. A curriculum was developed for this which, among other things, systematically addressed regulatory principles.

This approach is particularly important to the CHMP chair, who himself acts as a contributor on several topics. "The pilot project provides us with very good opportunities. We can now already say that the trend among the central licensing applications being submitted to the EMA in the coming years will very clearly be in oncological areas of indication," Enzmann stresses. "No other area is displaying this many new modes of action and active substances."

It's a win-win situation for all involved: "As regulators, we are conveying to the experts the basic principles relevant to oncological specialist fields. In so doing, we are giving them the basis so that they are able to bring their knowledge into the assessment of medicines in a targeted way." Principally, the HMA and EMA are assigned to have a close working relationship with academics and researchers: "In the licensing of medicines, we need to be prepared for future challenges and opportunities which arise from the advances in science and technology," stresses Enzmann. Especially when it comes to innovative treatments, which should be made available to patients quickly." •

“No other area is displaying this many new modes of action and active substances as do oncological indications.”

**Dr. Harald Enzmann,
Chair of CHMP**

PD Dr. Harald Enzmann

The medical doctor who gained a doctorate and achieved professor status has been a member of the committee for human medicines (CHMP) for the European Medicines Agency since 2005. In 2016, he was elected deputy chair of the CHMP. Since 2018, he has been chair of the board and in September 2021 was unanimously re-elected for a second term. He has been working at the BfArM since 2002. Here he headed, amongst others, the “medicines licensing” department. Since 2016, he has been the head of the “EU and international” office. Enzmann is a Fellow of the International Academy of Toxicologic Pathology, Member of the European Society of Toxicologic Pathology, the Society of Toxicology and the European Association for Cancer Research.

Drug Safety
Fluoroquinolones: On benefits and risks

If unwanted side-effects arise in a drug, mechanisms are put in place at an EU level to minimise risks. The BfArM brings its expertise to the committees of the European Medicines Agency (EMA). Fluoroquinolones are an example which demonstrates the need for long-term input: after sometimes irreversible side effects arose in its application, the BfArM repeatedly put these antibiotics to the test. And it was successful.

New findings on the safety of medicines can arise over the entire life cycle of a drug, therefore also a long time after their licensing. A significant tool for identifying possible risks in medicines is the close-meshed evaluation of reports of suspected side effects. If this results in a risk signal for a drug which is approved in several or all EU member states, processes are put in place at a European level for closer evaluation of such signals.

This is where Dr. Martin Huber comes in. He is the deputy chair of PRAC, the EMA Pharmacovigilance Risk Assessment Committee. PRAC works on the identification, assessment, minimisation and communication of drug risks. At the end of the process, the committee gives a recommendation on the drug‘s future.

Fluoroquinolones: highly effective, but not without risk

Drugs from the fluoroquinolone class have kept PRAC busy for some years. Fluoroquinolones are synthetic antibiotics which have a wide range of therapeutic applications. They have been in use for decades and play an important role in the treatment of severe bacterial infections. In addition to their antibiotic action, serious side effects have also been identified. In the worst

cases, these can be permanent. Infections, tendon tears, difficulty with eyesight, or depression have been among the described issues.

As some of the observed side effects can be long-lasting and possibly permanent, in 2017 the BfArM approved a European risk assessment process for fluoroquinolones. The aim of such a risk assessment is to check whether the benefit of a drug continues to outweigh the risks. This is performed based on the reporting of suspected side effects. In addition to this, experts evaluate the current scientific literature and other available data.

Far-reaching application restrictions

As a consequence of this process, the PRAC announced clear recommendations in 2018. Martin Huber: "There were far-reaching restrictions to the areas of application for fluoroquinolones; a few active ingredients even had their license rescinded. In addition to this, we have obligated the licence owners to update their product information so that they give information on the restrictions of approved application areas and on the application risks."

Members of health professions have been informed of the findings and recommendations of the process by way of a Direct Healthcare Professional Communication (DHPC). This concerns an important form of information for those working in the healthcare sector, which provides clarification on newly identified, significant drug risks and measures to mitigate those risks. In the case of fluoroquinolones, there had already been another DHPC issued which specifically addressed the risk of the incidence of aortic aneurysms and dissections. A further DHPC followed in October 2020 to draw attention to the risk of a cardiac valve regurgitation/insufficiency.

It has been known for some time that fluoroquinolones are associated with severe side effects. In the public domain, criticism is often made of the fact that, in spite of this, these antibiotics are still allowed to be used at all. "This is completely understandable," says Martin Huber. "But it needs to be said that fluoroquinolones are highly effective antibiotics with a wide range of therapeutic applications. In practice, they can be a treatment of last resort and therefore save lives. For example, once all other antibiotics have not worked or bacteria have developed resistance against other antibiotics." Doctors therefore need to weigh up on a case-by-case basis whether the benefit versus the risk of using medications containing fluoroquinolones are justified.

Prescribing behaviour under the microscope

Among the antibiotics, the fluoroquinolones, which are still authorised in Germany, were the fourth strongest class of active substances in 2021 with around twelve million defined daily doses. Fluoroquinolone antibiotics should only be prescribed for the approved indications and after careful >

weighing up of the risks and benefits. Martin Huber: “If we look at the previous application restrictions, it is clear that many are targeted as the treatment of last resort for patients. This means that there must not be any alternative therapeutic options available. The comparatively high prescription figures, however, suggest that fluoroquinolones are often used above and beyond these stipulations.”

The PRAC therefore decided to evaluate the introduced measures for risk minimisation using a medications application study. The study included data from six European countries, including Germany, and came to the conclusion that the number of prescriptions was slightly on the decline. While the interpretation of data from the medications application study is associated with restrictions, the observed tendency of a decline in the number of prescriptions in Germany is covered by other available data, such as the drug prescription report.

Monitoring after licensing

In particular during the period corresponding to the start of the risk assessment procedure and the resulting measures, a significant decline is recorded for Germany. “But we still cannot be satisfied with this,” says Martin Huber. “The study shows that fluorquinolones are still prescribed off-label.”

Against this backdrop, PRAC recommended a renewed DHPC letter in Spring 2023 to once more draw attention to the application restrictions and the severe side effects.

The fluoroquinolones are a good example of how strictly medications are monitored, even after licensing. At the same time, the latest scientific knowledge must be observed consistently in the prescribing behaviour. “The prescription of a drug – in this case an antibiotic – is a decision made by a medical professional for a specific patient,” Martin Huber stresses. “Application risks therefore always have to be discussed on an individual basis. The BfArM will continue to provide its expertise here, so that the knowledge of drug risks grows and patients can receive optimal and safe treatment.” •

“The study shows that fluoroquinolones are still prescribed off-label.”

Dr. Martin Huber,
Deputy chair of PRAC

Dr. Martin Huber

Studied Pharmacy at the Goethe University Frankfurt am Main, as well as postgraduate studies in health sciences – Public Health at the Technical University Dresden. Started as a scientific member of staff, including in hospital. In 2010 he switched to the BfArM in the pharmacovigilance department. Involvement in the working groups and committees at European level from an early stage. Member of PRAC since 2012. Deputy chair of this committee since 2018.

Medical Devices

From the case file to the prototype

The broad and highly dynamic field of medical devices is shaped by leaps in technology and innovation. Alongside this are processes for accessing the market and in risk assessment which are largely based on manually created tables and texts – the contrast could hardly be any greater. In order to close the gap between the dynamic world of technology and the current reality of assessment, the BfArM brings targeted expertise of risk processing and assessment of medical devices to forward-looking initiatives. With in-house research into data-protected detection and assessment of risk signals, the Federal Institute is taking a pioneering role among the European authorities.

We are already beginning to see where digitalisation will be revolutionising patient care: products are becoming increasingly targeted towards individual groups, digital assistants and the like are part of everyday life, while communication about products is growing. “Medical devices are becoming increasingly smart and connected,” says Dr. Samet Bayraktar from the Department of Medical Devices. “The more sophisticated they become, the more complex they are too. This is true for the entire life cycle, from development, certification and market access, to risk reporting assessment and monitoring. This increases the challenges for all players involved.”

Manufacturer information and documentation generally includes several pages of text, hundreds of lines of tables and countless references. To check this in detail is time-consuming and labour-intensive.

Together with his colleague Dr. Davood Moghadas, Bayraktar works as a Data Scientist for the BfArM. Their mission: to set up data in a structured way, enabling interfaces between the processes, and creating the groundwork for supporting IT tools. For this, the BfArM is, among other things, involved in two research initiatives: AI-assisted certification of medical software (KIMEDS) and Secure Medical Microsystems and Communications (SEMECO). Both projects benefit from regulatory expertise and a wide range of data through which the BfArM has access to event reports for medical devices. The data scientists at the BfArM are agreed that making this treasure trove of accessible knowledge would be to the benefit of developers, certification authorities and, above all, also the patients.

Accelerating processes, increasing safety

More than 35,000 risk reports on medical devices are received by the BfArM every year – and the trend is on the rise. In each case, the assessors need to be in a position to gain a comprehensive overview of the problem and its causes as quickly as possible, so that they can make informed decisions on any measures required with regard to patient safety. The more comprehensive the safety documentation becomes, the greater the risk that relevant safety problems could be missed. “In the KIMEDS project, to put it simply, we are therefore looking into the approach of allowing manufacturer documentation on safety aspects to be checked using the help of artificial intelligence (AI),” explains Davood Moghadas. “This can speed up the assessment and, at the same time, increase the level of analysis.”

The BfArM is relying on data and text mining. This involves statistical methods being applied to the ample data stocks. Davood Moghadas: “The aim is to transfer our individual cases into a network of information with logical connections. >

“Medical devices are becoming increasingly smart and connected.”

**Dr. Samet Bayraktar,
Data Scientist in the medical devices department, specialising in research, data management and analytics**

Dr. Samet Bayraktar

Studied biochemistry at the Heinrich Heine University Düsseldorf (HHU), with subsequent doctorate in Münster. From 2015, various positions in the Münster university hospital with training focussing on machine learning and artificial intelligence. Since 2021, working at the BfArM as Data Scientist in the medical devices department, specialising in research, data management and analytics.

This allows us to detect patterns and trends that will help us in our regulatory work. This kind of accessible pool of knowledge will enable us to analyse newly reported events much faster and better. At the same time, weak points and potential sources of errors can be identified in advance in a more targeted way – for example, during clinical examinations."

The vision of KIMEDS: a process supported by artificial intelligence over the entire life cycle of a medical device. Access to market will be facilitated for developers, while certification bodies, supervisory authorities and the BfArM will be able to carry out analysis and evaluation faster, in greater detail and in a more targeted way. Patients will get double the benefit. "On the one hand, new, innovative products reach the market more quickly and, on the other hand, the data-supported processes improve safety," Moghadas explains.

KIMEDS initially focussed on medical software for X-ray machines and endoscopes. In the long term, AI-supported evidence has the potential to have a positive influence on the entire medical device sector.

Certification meets cybersecurity

How valuable structured knowledge can be, becomes apparent at the latest when the technical medical evaluation is performed in conjunction with cybersecurity. This where the SEMECO project comes into play, expanding the knowledge modelling or the basic methods of KIMEDS with the cybersecurity topic. "We are all familiar with media reports about hacker attacks, which can bring whole hospitals to their knees," says Bayraktar. Of course more communication and connectivity also for medical devices and their components means more potential targets for attackers. On the one hand, functional flexibility is needed, but it is becoming increasingly difficult and time-consuming to provide formal evidence for the security. "Manufacturers need to get deeply involved in the development and also cover areas outside of their own core competences," says Bayraktar, highlighting the problem. The SEMECO project is therefore dedicated to medical microsystems and searches for solutions to bring system development and security documentation in line with each other.

Structuring diversity

The aim is to create a new ecosystem using a modular design of system, modular platform and modular regulations. Samet Bayraktar: "In the project, we want to work together with other project partners from research, regulation and industry to create a kind of construction kit, which guarantees standards for regulatory documentation using scalable knowledge systems and explicable artificial intelligence." Currently, electronic circuit designs and chip designs exhibit minimal standardisation and high variability. Since all medical microsystems are software-controlled, it stands to reason that safety documentation should already be integrated at a system software level. >

Structured knowledge also has a key role to play here. As a regulatory player, the BfArM identified cases in its incident database which are related to cybersecurity. “From the infusion pump to the pacemaker, we have many application cases which could be relevant to this topic. We aim to generate as seamless a picture as possible to filter out patterns and logical correlations here too,” says Bayraktar. As with KIMEDS, this structured knowledge represents a treasure trove of experience which helps to identify potential weak spots in advance, and to be able to better contextualise known problems and solve them.

So that research plans also have a lasting impact, the BfArM also brings the approaches to the European committees on medical device vigilance and to clinical trials as well as into the heart of the International Medical Devices Regulators Forum (IMDRF). This engagement across borders is important, as developers and manufacturers are usually at home on the global market. The BfArM is therefore the driving force behind European and international standardisation. In any case, it is also a matter of global interest: traditional processes, which are literally represented by old case files, need to be adapted to the extremely dynamic developments of the products. Because with the high speed that technological progress purports to and demands, players such as the regulatory authorities otherwise run the risk of losing their capacity to act.

The two data scientists, Bayraktar and Moghadas, are therefore convinced of this: “We need to pick up this tempo and become drivers of innovation ourselves.” With KIMEDS and SEMECO, the BfArM is taking on precisely this pioneering role and taking advantage of the possibilities for how technological progress can remain controllable with the help of its own achievements. •

“More than 35,000 risk reports on medical devices are received by the BfArM every day – and the trend is on the rise.”

**Dr. Davood Moghadas,
Data Scientist in the medical devices department, specialising in research, data management and analytics**

Dr. Davood Moghadas

Studied geophysics at the University of Tehran (Iran). Doctorate at the Jülich research centre (FZJ) in collaboration with the Université catholique de Louvain (UCLouvain, Belgium). Most recently working as lecturer and data manager at the Brandenburg University of Technology Cottbus–Senftenberg (BTU), also with a focus on machine learning and artificial intelligence. Since 2021, at the BfArM as Data Scientist in the medical devices department, specialising in research, data management and analytics.

Rare Diseases
The invisible ill

In Germany, there are no exact figures on the number of people suffering from “Rare Disease”. Estimates are around four million people. The exact figure remains unknown, because the healthcare system does not have a precise coding for many of these diseases. A problem with far-reaching consequences: without precise data, healthcare policy is missing an important decision-making basis. The BfArM wants to change this – partly to enable research and new therapies.

The problem lies in the system. More precisely in the medical coding system. This system maps diseases using a letter code known as the "international classification of diseases", or ICD, and is in use globally. Using this code, the health insurers, for example, can determine how often certain diseases occur, which treatments are being prescribed and, above all: what these treatments cost. Coding a disease is therefore an important basis for decisions in healthcare policy.

No clear ICD code

But what happens if a disease cannot be assigned a unique ICD code? "This makes those affected literally invisible in this system," explains Carina Thomas. The medic works in the "Coding system and register" department of the BfArM. The Federal Institute is involved in the care and further development of the ICD code as one of the WHO cooperation centres. The coding system has already been revised a few times since its launch by WHO in 1983. The eleventh version, the "ICD-11" is currently in its introductory phase.

These ongoing expansions and revisions are, among other things, to allow diseases to be coded more differentially than before. Because if codes cover numerous different diseases, it is impossible to specifically identify individual diseases. These differentiations are also crucial for people suffering from a Rare Disease. "Currently, around 6000 to 8000 of these diseases are known," explains Thomas. "But the ICD only provides specific codes for around 500 of these. The remainder are assigned codes which are also allocated to other, more common diseases."

This is a problem for those affected, because precise diagnostic information is highly relevant to health services research and the planning of clinical trials, and thus the development of new therapies. Information, too, which aims to facilitate everyday life for these patients, needs to be clearly assigned. Another example is in provision: the gaps in data make it hard to detect where Rare Diseases are often treated and, based on this, where special expertise is available for their treatment.

Orphanet registers Rare Diseases

Therefore, in order to make all Rare Diseases visible in the coding system, in Europe it is recommended that ORPHAcodes by Orphanet be used. Orphanet is an international reference database which provides information on Rare Diseases and their treatment with corresponding drugs (Orphan drugs). Orphanet meanwhile has more than 6000 Rare Diseases, each with their own ORPHAcode.

However, ORPHAcode needs to be used in addition to the obligatory ICD coding. This means that it is possible for a disease with a specific ICD code to have more than one ORPHAcode and vice versa. Because of these factors and the additional work of using two systems, the national project "Coding Rare Diseases" was launched. The aim was to link ICD-10 codes and Orpha identification numbers. To do this, both systems >

where prepared in a common file, known as "Alpha-ID-SE". When using this, selecting the name of the disease once provides both codes.

The national Orphanet team

The BfArM has been an Orphanet project partner since 2021 and Carina Thomas is part of the national Orphanet team. She works here on implementing the Alpha-ID-SE into the healthcare system. This includes the maintenance and preparation of the annually updated version of this file. In order to promote its use, the BfArM is also offering training, talks and webinars. Furthermore, employees collect data on available specialist provisions such as expert centres, medical laboratories with testing facilities, ongoing research projects, clinical trials, patient registers and patient organisations. They are entered into the Orphanet database and can then be called up via the central website.

"At a national level, we are in close discussion with interest groups and participate in numerous EU projects," says Thomas. "We work together to improve the visibility of Rare Diseases in the healthcare system."

Full data can save lives

The clear coding of Rare Diseases using Alpha-ID-SE has been mandatory in hospitals since 2023. This data then flows into the research data centre so that it is available for research queries. In future, the coding could also be expedient in the outpatient area. The ORPHAcodes could also be used in the electronic patient file, e.g. to give the user specific tips on therapies for the Rare Diseases patterns.

"Full data and algorithms can save lives and contribute towards a better quality of life," stresses Carina Thomas. "This requires further incentives in drug research and the digitalisation of medical facilities. The common aim is to create the accompanying digital healthcare structures – and our work on the coding system is an important building block for this." •

“We work together to improve the visibility of Rare Diseases in the healthcare system.”

Carina Thomas,
Acting line manager
of the K4 specialist field

Carina Thomas

Studied human medicine at the University of Mainz & University of Cologne 2002 – 2009. Medical work in the general and vascular surgery clinic in Leverkusen and the Marien hospital in Bergisch Gladbach 2010 – 2021. Started working as a scientific officer in the specialist field of K4/Orphanet Germany 12/2021. Deputy line manager of the K4 specialist field in 06/2022. Acting line manager of the K4 specialist field in 06/23.

Real-World Data
Expanding the horizon for better medicines

Ten partner institutions from Europe are participating in the Real4Reg project, which is being coordinated by Dr. Silja Wortberg for the BfArM. Large data volumes from healthcare and artificial intelligence aim to improve regulatory processes.

Every day, a great quantity of data is created in healthcare: such as accounting data from health insurers, data from registers (for example the individual Federal states' cancer registers) or even data from electronic health files. Known as Real-World Data (RWD), these also offer a great opportunity for regulatory decision-making. Randomised Controlled Trials (RCT) are accepted as the gold standard to prove the efficacy of a new drug and to approve the product. But these trials also have their downsides, as the trial conditions do not reflect the real world. Trial participants are generally young, healthy men, which makes it difficult to transfer the results to other patient groups, such as older people, women of all ages and children. Furthermore, for ethical reasons, it is difficult to carry out clinical trials for population groups such as pregnant women

or children. It is also very difficult to reach the necessary large case numbers for RCTs for people with Rare Diseases.

Improving regulatory processes

This is why RWD is a great opportunity, as it represents the reality of the everyday treatment of the population. At the beginning of 2023, the research project Real4Reg was launched, initiated and coordinated by the research department of the BfArM and promoted by the European Union (Horizon Europe Programme). The aim of the project is to improve regulatory processes in the authorities using RWD. This means that regulatory and Health Technology Assessment (HTA) bodies are provided with optimised methods for the effective exploitation of RWD for the assessment of medicines. "In this way, we expand the horizons of regulators over and above the clinical trials," explains Silja Wortberg, talking about the project. To do this, accounting data from health insurers and data from national registers should be used. Another aim of the project is to further develop methods for the suitable application of artificial intelligence (AI) on RWD sources in the context of the regulation and Health Technology Assessment (HTA). To be able to tackle the huge quantity of data, artificial intelligence is to be used for the analysis and evaluation, in order to identify patterns and prediction models. In addition to classic statistical models and propensity score algorithms, a wide range of AI algorithms and methods are therefore also applied.

The first challenges

In addition to the BfArM, another nine organisations from six European countries are participating as coordinators. These include HTA bodies, academic institutions and patient organisations. At the beginning of the project, Wortberg reports: "Our first challenge is to have common standards so that the data from the various countries can actually be used as a data set in the first place." Coordinated by the BfArM, the data from the European partner countries is to be converted into a common data model so that it can be used for joint assessments. "This data also forms a very important basis for further cooperation as part of the European Health Data Space (EHDS) or DARWIN EU," explains Wortberg.

A huge data foundation

In Germany, the project plans to use data, among others, from the Health Data Lab. This is currently being set up at the BfArM. It receives the data from all of the around 73 million people with statutory health insurance in a pseudonymised form, which is collected and quality-assured by the German National Association of Health Insurance Funds (GKV-SV), and can then provide this on request in an anonymised or pseudonymised form for the purposes of research and improving healthcare provision. To guarantee the protection of the data, the Real4Reg project does not exchange data between the organisations originating from different countries. >

The BfArM as coordinator for Europe: Improvement in regulatory decision-making using real world data and artificial intelligence.

Project topics

The Real4Reg project kicked off working with four relevant application examples from regulatory practice along the product life cycle of medicines: Amyotrophic Lateral Sclerosis (ALS), breast cancer, SGLT2 inhibitors and fluoroquinolones. Using the application examples, studies are conducted into the use of RWD to describe trial populations, the use of historic controls/digital twins, the analysis of RWD for evaluating drug safety as well as for addressing efficacy and drug repurposing.

In addition to the application of classic evaluation methods, project partners the Fraunhofer Institute for Algorithms and Scientific Calculations (SCAI) and CSC Finland develop AI algorithms and methods, the benefits of which can be used for regulatory decisions in these topic areas. If this works, the scripts can in future be transferred to other topic areas and application examples.

The project continues to work on strategies concerning how these new approaches can be introduced into the regulatory and HTA authorities in Europe. Wortberg explains: “The structure and approach of our project targets the implementation of effective data exploitation from ’the real world‘ outside of clinical trials to facilitate decision-making in the context of regulation and HTA evaluation.” For this purpose, a survey is carried out as part of the project, which queries the requirements and wishes of the relevant European stakeholders, so that the results of the project can be converted into training measures which are right on target.

The participants give up-to-date information on the current status of the project on the real4reg.eu website. The first results are expected to be published in 2024, while the project should run until the end of 2026. In addition to training measures for the application of RWD in a regulatory context, the project results are relevant for existing and arising guidelines for regulatory bodies in healthcare and HTA bodies across Europe.

“Ultimately, the efficacy and safety of medicines should be increased.”

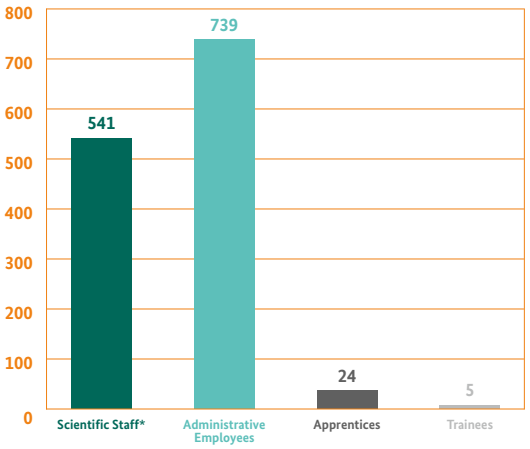
Dr. Silja Wortberg,
Project Coordinator Real4Reg

Dr. Silja Wortberg, Project Coordinator for Real4Reg

Studied medicine, psychology and sociology. 2006 to 2012, worked as research assistant for the Federal Centre for Health Education (BZgA) in the department of infection protection; scientific officer at the German Institute for Addiction and Prevention Research (DISuP) as well as at the Cologne and Witten/Herdecke universities, has a doctorate in health sciences. Since the end of 2021, research coordinator in Department 5 of the BfArM.

Data & Statistics
The BfArM in figures

BfArM as employer



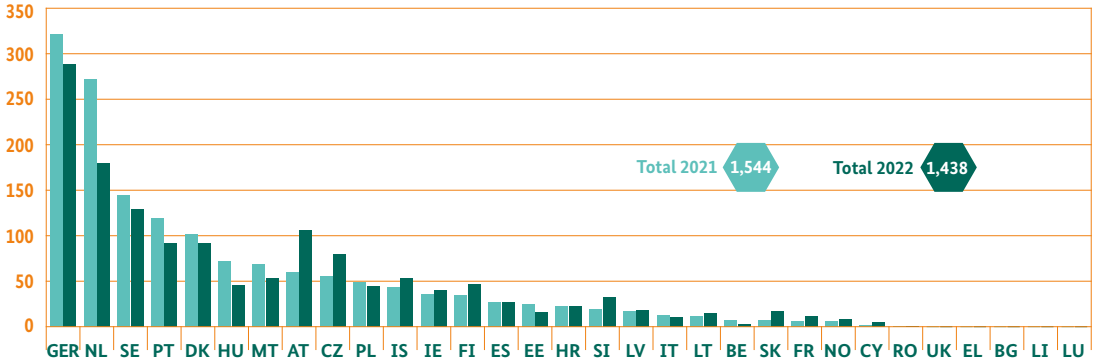
*) excluding lawyers, IT and administrative staff in senior positions

The BfArM is the largest European body in the area of licensing and safety of drugs and medical devices. Around 1,300 employees in a wide range of disciplines are committed to the safe care of patients.

Of the scientific staff members, around 31 percent are pharmacists; around 22 percent are medics; almost half (around 47 percent) are made up from scientific professional categories.

Drug approval

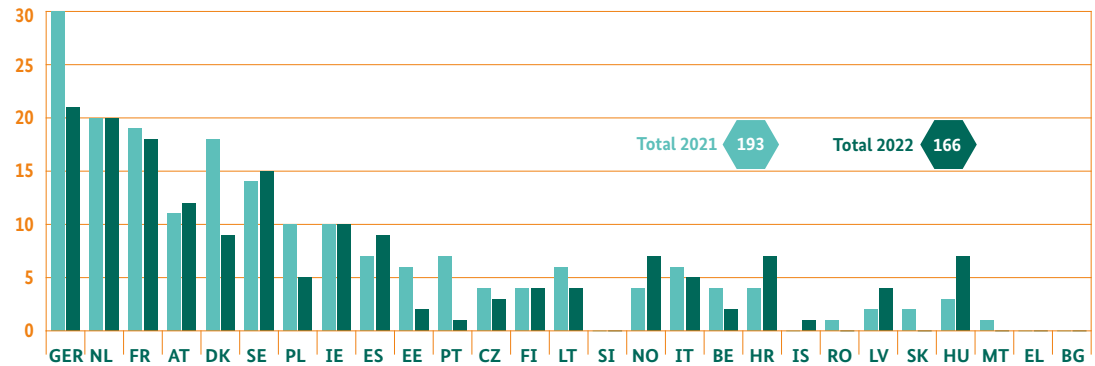
Decentralised licensing processes: leading procedures BfArM



The BfArM has confirmed its leading position over recent years in the European network of all licensing bodies for medicinal products. During the Covid-19 pandemic, the BfArM fully continued its processing of procedures as a Reference Member State (RMS) despite many additional tasks. The RMS is responsible for lead processing.

In 2021, the BfArM looked after 21 percent of all EU procedures carried out decentrally as an RMS. This includes the DCP (Decentralised Procedures) and Mutual Recognition Procedures (MRP). In 2022, as an RMS, the BfArM participated in 20 percent of all EU procedures carried out decentrally.

Central licensing procedures via the European Medicines Agency (EMA)



The BfArM also takes on a leading role in the centralised licensing processes for innovative medicines. Licensing of the appropriate medicines for these procedures automatically applies for the whole of the European Economic Area – unlike for the decentralised procedure. In 2021, Germany provided the rapporteur or co-rapporteur for 30 centralised procedures, which is the reporting or leading authority (The BfArM and Paul-Ehrlich Institut, PEI). In both 2021 and 2022, the BfArM was lead manager for 15 procedures. In 2021, it also supported the PEI, which was responsible for vaccines, in individual procedures with the assessment of the vaccine quality.

288,845

suspected cases of side effects have been reported by Germany to the European Medicines Agency (EMA) in 2022. A total of 1,193,132 reports were received by the EMA.

109

applications for acceptance into the DiGA register received by the BfArM in 2021 and 2022. 32 applications were accepted after testing.

110

years of the semen donation register, which stores the personal data of semen donors and recipients in connection with medically supported artificial inseminations.

600

first applications for approval of a clinical trial processed by the BfArM in 2022.

210

consultations on digital healthcare applications (DiGA) performed by the BfArM in 2021 and 2022.

12

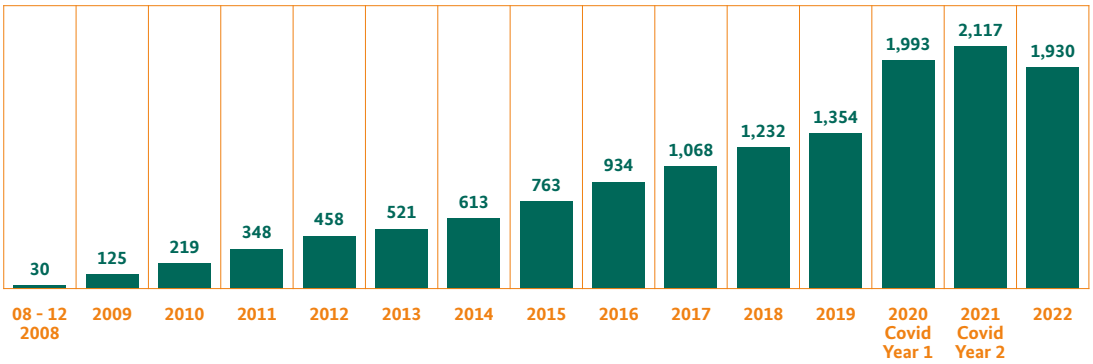
GCP inspections (Good Clinical Practice) performed by the BfArM in 2021 and 2022.

42

reports of suspected fraudulent cases were received via the international early warning system in 2022, largely discovered outside of the legal supply chain.

German Clinical Trials Register (DRKS)

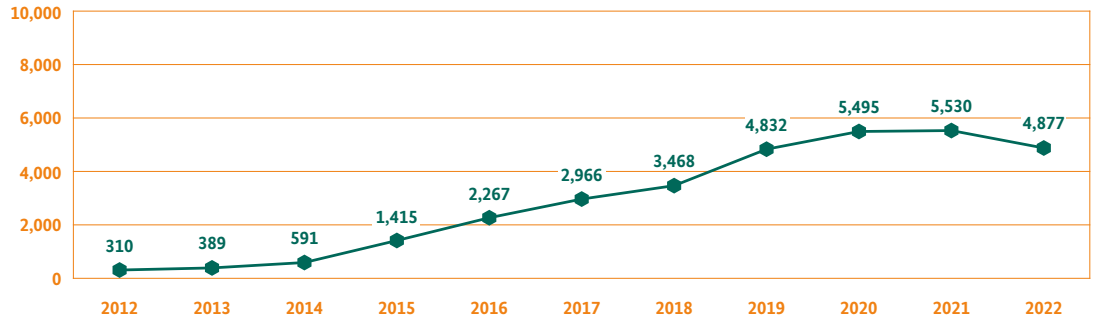
Registrations performed each year



The German Clinical Trials Register (DRKS) is recognised by the World Health Organisation WHO as the primary register for Germany. It is responsible for the registration of all patient-oriented clinical trials carried out in Germany. The aim is to provide the public with a full, current overview of all clinical trials being carried out in Germany. The DRKS is an independent provider with public funding, which is operated by the BfArM. At the end of 2022, the register covered around 13,500 trials and recorded constant growth. Since 2016, the number of registrations has virtually doubled.

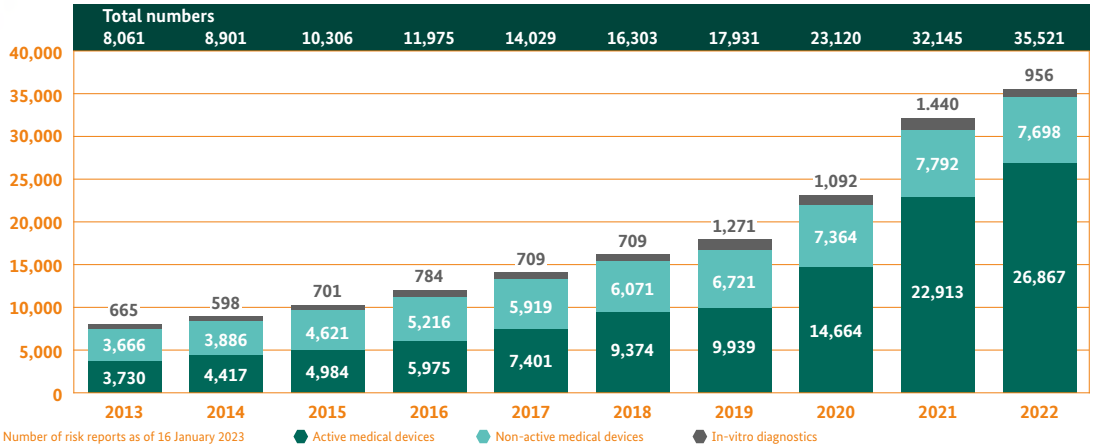
Reporting side effects

Direct reports from Germany from patients



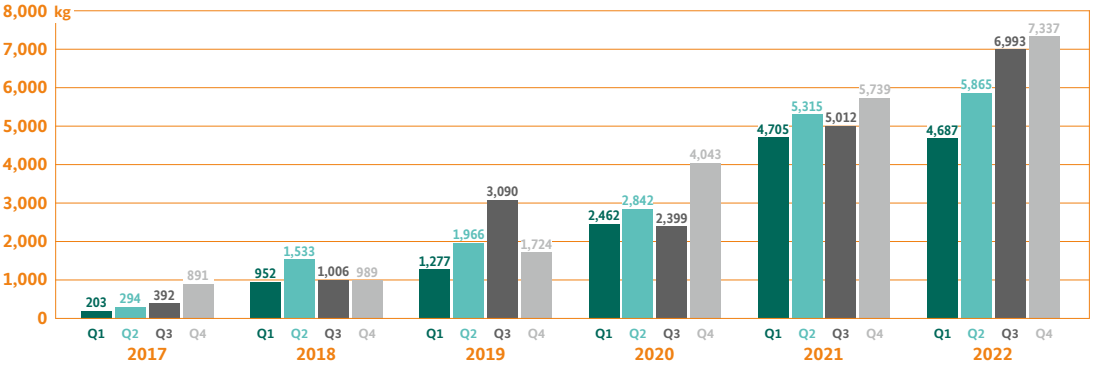
In conjunction with the PEI, the BfArM provides the online portal www.nebenwirkung.bund.de, where adverse drug effects can be reported. Each report is quickly, directly and safely received from there by the experts from both authorities. Important: it is not only members of the medical profession who can report adverse events; patients and their family members or representatives may also do so. The BfArM has itself recorded continuous and significant growth in the number of direct reports. For example, reports by patients, their family members or representatives have grown 16-fold in the past ten years.

Risk reports for medical devices



In the case of medical devices, the main task for the BfArM is the risk assessment of incidents. Manufacturers, authorised representatives and importers as well as users and other distributors are duty-bound to report incidents with medical devices to the BfArM in accordance with the provisions of the Medical Device Safety Plan Ordinance (MPSV).

Cannabis imports for medical and scientific purposes



Medical cannabis may in principle be imported from any country, which carries out the cultivation of cannabis for medicinal purposes under state control in accordance with the Single Convention of 1961 on Narcotic Drugs and is able to offer cannabis in medicinal quality. The Federal Opium Agency at the BfArM issues the required permissions and licenses to companies interested in importing medicinal cannabis, however it does not have any centralised controlling role. It also has no influence on whether and to what extent the entitled companies are actually importing cannabis.

20

DHPCs have been published by the BfArM in 2022.

15.7 Mio

anaesthetic prescriptions issued by the BfArM to doctors in 2022. The trend continues to rise slightly.

290

national scientific consulting processes performed by the BfArM in 2022. This could include: advice in the development phase, before requesting a clinical trial or before applying for a license.

788

hectares cultivated for opium poppies (papaver somniferum) in 2022. First a reduction, after which the annual cultivated area reached a peak in 2021 with 1077 hectares.

970

reports of possible batch-related defects processed by the BfArM in 2022. This resulted in 75 recalls.

33

total number of kick-off meetings performed by the BfArM Innovation Office in 2021 and 2022. Academic research groups, small and medium-sized enterprises as well as start-ups have the option here to receive guidance on early medicines and medical device development.

Around 105,000

marketable medicines are under the BfArM‘s area of responsibility in Germany (as at July 2023).