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Initiative: Advancing
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Luxembourg
10–12 May 2023

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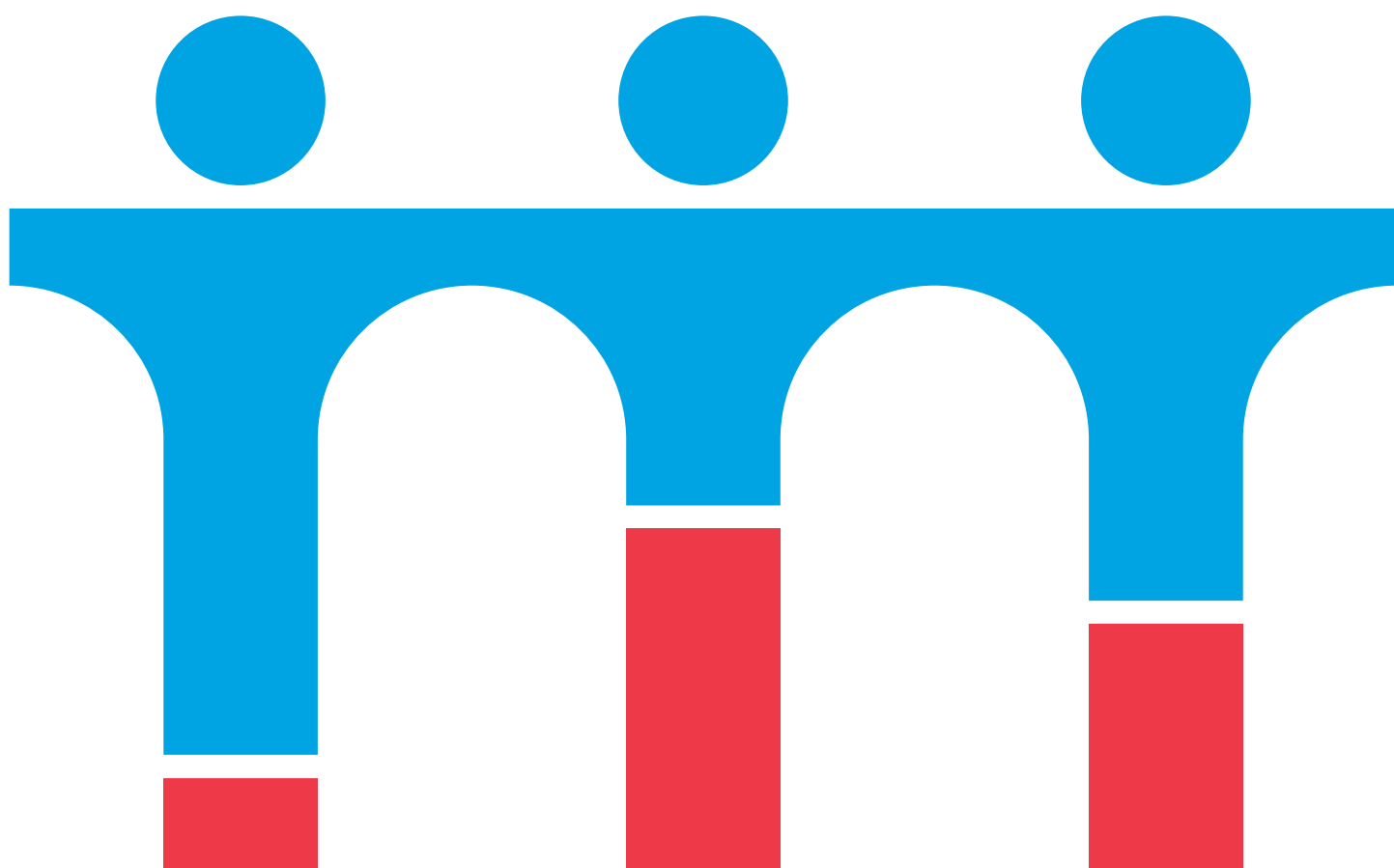


**World Health
Organization**

European Region

Issues and challenges in access to medicines faced by small countries in the WHO European Region

Policy brief



Issues and challenges in access to medicines faced by small countries in the WHO European Region

Policy brief

Abstract

Essential medicines save lives and improve health when they are available, affordable, of assured quality and properly used. Lack of access to essential medicines is one of the most serious global public health problems and many new medicines are becoming expensive even for the health systems of high- and middle-income countries. This policy brief focuses on the issues and challenges in access to medicines faced by the 11 countries of the WHO Regional Office for Europe Small Countries Initiative. Many of these countries' challenges arise from or are aggravated because of the size of their pharmaceutical markets. Small countries have low negotiating power and country-specific requirements such as producing tailored health technology assessment (HTA) and pricing and reimbursement dossiers, packaging and leaflets in local languages also decreases the appeal for marketing products in small countries. Furthermore, development of HTA, managed entry agreements and horizon scanning processes requires resources and specialized knowledge and skills often less available in small countries, leading to less favourable procurement terms for public payers. The strategy to address these issues and challenges is through voluntary cooperation, on joint horizon scanning, pooled demand and procurement, and HTA integration, which the Access to Novel Medicines Platform can support.

Keywords

ACCESS TO MEDICINES, PHARMACEUTICAL POLICY, MEDICINE, HEALTH SYSTEMS, DRUGS, PUBLIC HEALTH

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Abbreviations

EFPIA – European Federation of Pharmaceutical Industries and Associations

EU – European Union

HTA – health technology assessment

HTAR – Regulation on health technology assessment

IHSI – International Horizon Scanning Initiative

MEA – managed entry agreement

NMP – Access to Novel Medicines Platform

SCI – Small Countries Initiative

Introduction

Medicines save lives and improve health when they are available, affordable, of assured quality and properly used. Lack of access to essential medicines remains one of the most serious global public health problems, however. So far, discussions about this pressing issue have mostly focused on low- and middle-income countries, where it is most pronounced. WHO estimates that about 30% of the world's population (mostly residing in these countries) lack regular access to essential medicines, while in the poorest parts of Africa and Asia this figure rises to over 50% (1). Nevertheless, difficulties with access to medicines abound in other countries as well. For instance, many new medicines are becoming too expensive even for the health systems of high-income countries (2), and other issues such as shortages of essential – often older – off-patent and generic medicines are becoming a worldwide crisis (3).

This policy brief focuses on the issues and challenges in access to medicines faced by the 11 member countries of the Small Countries Initiative (SCI) of the WHO Regional Office for Europe. The SCI was established in 2013 as a platform through which 11 countries in the WHO European Region with 2 million inhabitants or fewer can work together to address common issues and share experiences to improve population health in their countries. The participating countries are Andorra, Cyprus, Estonia, Iceland, Latvia, Luxembourg, Malta, Monaco, Montenegro, San Marino and Slovenia.

Many of the challenges they face in access to medicines are primarily generated or are further aggravated because of the modest size of their pharmaceutical markets. The discussion of common issues draws upon published research and remarks highlighted by country representatives during a virtual policy dialogue held by the Regional Office on 8 March 2023 (4).

The policy brief also aims to identify potential solutions for the most pressing problems on increasing cooperative efforts, and to highlight how the Regional Office can support countries via collaboration or by convening conversations with the private sector and other non-State actors through its Access to Novel Medicines Platform (NMP) (5).

Issues and challenges faced by small countries

Shortages and lack of availability of novel medicines

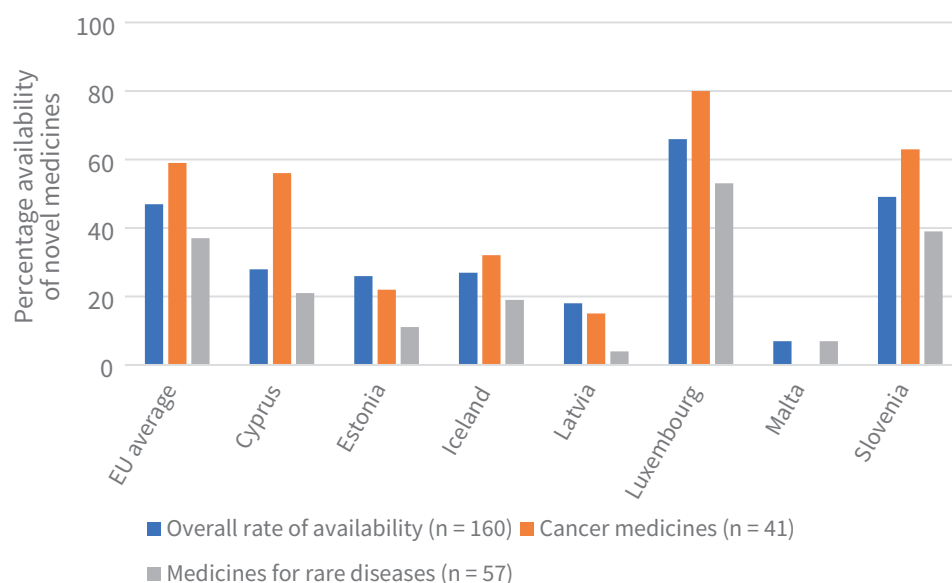
In recent decades, not only have novel medicines improved survival rates and quality of life for many patients around the world, but some have also positively changed the natural history of diseases such as HIV, hepatitis C and certain cancers (6). The draft pharmaceutical strategy for Europe of the European Union (EU) notes, however, that innovative and promising therapies do not reach all patients because of different levels of access to medicines in different countries (7). At the time of writing, this draft strategy seeks to provide incentives for companies to market a medicine in all EU countries.

Significant inequity in access to medicines exists across the WHO European Region because companies can decide not to market their medicines in a particular country, or can withdraw them from one or more countries, according to their marketing plans. This can be caused by various factors – such as national pricing and reimbursement policies, population size, organization of health systems and national administrative procedures – and it results in these problems being faced by smaller and less wealthy markets in particular. These issues are even more pronounced in small countries in the Region that are not in the EU, and thus do not benefit from centralized authorization procedures or joint EU initiatives targeted at improving access.

A number of reports testify to the stark differences in access to novel medicines between European countries. A study from the European Society for Medical Oncology revealed that oncology treatments are more often available and covered in western than in eastern European countries, where many drugs are either not available or only available at full cost to patients (8). Substantial differences in access have also been reported for medicines for rare diseases: country expenditure on these treatments varied between €0.2 and €31.9 per inhabitant (9), again with a notable disparity between the eastern and western parts of Europe.

The European Federation of Pharmaceutical Industries and Associations (EFPIA) published a dataset on the availability of novel medicines authorized by the European Medicines Agency from 2017 to 2020 (160 in total) as of 1 January 2022. The dataset indicates that most member countries of the SCI for which data are available (except for Luxembourg and Slovenia) are behind the EU average in terms of availability of novel medicines, including cancer medicines and medicines for rare diseases (Fig. 1).

Fig. 1. EFPIA data on availability of novel medicines registered by the European Medicines Agency from 2017 to 2020



Source: EFPIA (10).

These data need careful interpretation, as other treatment options may be available, and work on the issue is ongoing through the NMP. Differences in availability may result from issues on both sides of the market – with payers and industry (5, 11) – and may include:

- high prices imposed by monopolists (as novel products from industry are patent protected);
- national budget priorities and/or willingness and/or ability to pay;
- sequential launch strategies, which are commercial decisions;
- differences in value assessments; and
- differences in health technology assessment (HTA), pricing and reimbursement process and timelines.

While small countries may experience all these contributing factors, they are also deprioritized in the launch of new products because of their small market sizes. According to EFPIA (11) application for pricing and reimbursement is a time-consuming process. Every country requires the manufacturer to develop a tailor-made dossier in the local language and in compliance with local rules. Although companies often have specialized groups to manage this process, it is still necessary to prioritize internal activities. This issue is exacerbated for smaller companies that have not gone through the process before, and for companies that have not launched a new medicine for some time. As with any commercial decision, and in many sectors of industrial production, companies take into account the commercial size of the opportunity to determine where to put their resources. This has been corroborated by research that has observed significant and robust market size effects that decrease the launch time of new pharmaceutical products as market size increases (12) and previous WHO reports (13). This issue is being addressed by the draft EU Pharmaceutical Strategy which provides incentives for launch in all 27 EU Member States (7).

Key issues specific to small countries

- Pharmaceutical companies consider the commercial size of opportunities when deciding how to prioritize countries when applying for marketing authorization and reimbursement of novel medicines. This can lead to a lack of availability in small markets.
- The obligation to produce HTA, pricing and reimbursement dossiers in the local language and based on local requirements demands efforts and investments that are less appealing in small countries owing to modest expected volumes of sales.
- Capacity for HTA, pricing and reimbursement.
- Overall budget.

Shortages and lack of availability of essential medicines

Lack of industry interest in registration and reimbursement of medicines in small countries for commercial reasons is not limited to novel medicines but also extends to generics and biosimilars. Competition from and between these medicines is expected to be a major driver in cost containment in most European countries, facilitated by internal therapeutic price referencing. This issue could be contributing to relatively higher prices of medicines overall in smaller countries. In addition, the availability of fewer generic (such as antibiotics) and biosimilar products in the market increase the chances of shortages, which are particularly problematic for medicines that are not attractive to pharmaceutical companies – such as older, off-patent and generic medicines, which are less profitable because of low prices.

A study commissioned by the European Commission in 2010 (14) found that countries with larger populations, higher levels of pharmaceutical sales, greater expenditure on health as a percentage of gross domestic product and larger pharmaceutical market capitalization had a larger number of generics on the market. This means that reasons for low generic entry include not only medicines with low sales but also small markets in terms of patient populations.

Another major barrier to entry identified for generic manufacturers was the cost associated with placing the product on the market. Companies noted that the costs of both translating dossiers for marketing authorization and having to produce small amounts of country-specific packaging and leaflets led to diseconomies of scale. Other causes of generic unavailability identified by the study were not specific to small markets, but may nevertheless have more severe consequences for small markets. These included pricing and reimbursement policies and measures at the country level that discourage generic manufacturers from launching their products, such as regulatory policies that do not favour generics – including those related to prescribing, dispensing, reimbursement and pricing. The results of an econometric regression analysis carried out during the European Commission’s inquiry in the pharmaceutical sector in 2009 (15) confirm that high sales value is associated with a higher likelihood of generic entry.

It should be noted, however, that evidence in the literature on the extent to which smaller countries suffer from higher prices of generics is mixed. For instance, Kocheva et al. reported on high prices in Malta (based on a sample of medicines used for cardiovascular and respiratory diseases) but low prices in North Macedonia and Slovenia, compared to England, United Kingdom (16). Garouliene et al. (17) reported that it is possible for European countries with smaller populations to engineer low prices with manufacturers. This was seen among classes of medicines with limited utilization in Lithuania versus western European countries, as well as among classes with similar utilization patterns. Overall, it appears that sound pharmaceutical pricing policies can lead to low prices of generics even in smaller markets, while again noting that generic companies may be disproportionately disincentivized from registering new products and applying for reimbursement in these countries – particularly if they are not appropriately accompanied by policies to increase use of generics.

Key issues specific to small countries

- Pharmaceutical companies consider the commercial size of opportunities when deciding how to prioritize countries when applying for marketing authorization and reimbursement of generics and biosimilars. This can lead to a lack of availability in small markets.
- Having to produce small amounts of country-specific packaging and leaflets leads to diseconomies of scale in small markets, further decreasing the appeal for marketing products in these countries.
- Pricing regulation and pharmaceutical policies may disproportionately disincentivize companies from registering new products, including generics and biosimilars, and applying for reimbursement in small countries owing to comparatively lower expected volumes of sales.

Limited negotiating power resulting in higher prices of novel medicines

A previous WHO report noted that not all public payers have the same level of negotiating power with pharmaceutical companies (13). Market size (from the manufacturer’s perspective) and reliance on a competent HTA institution (which can benefit a payer at the negotiation table) are reported to have significant impacts. This is important because, as well as needing a political decision, development of capable HTA institutions requires investment and sufficient staff (18) with specific knowledge that may be difficult to find and recruit in small countries. As a consequence, not all countries in the WHO European Region have mechanisms in place to evaluate the cost-effectiveness of new drugs, which hampers value-assessment and decision-making processes to the detriment of patients at the national level. While joint HTA activities have been conducted among countries in the EU on a voluntary basis in the past (19), and as of January 2025, it will become mandatory for the assessment of relative clinical effectiveness and relative clinical safety (but not the health economic aspects of novel medicines) for a small number of novel medicines under Regulation (EU) 2021/2282 of 15 December 2021 on health technology assessment (HTAR), the same opportunity does not exist for other countries in the WHO European Region (20).

While plausible, the assertion that small countries pay more for novel medicines due to weaker negotiating power is difficult to prove, as most developed countries procure these products through confidential

agreements – including managed entry agreements (MEAs) – that conceal net prices to avoid them being used to benchmark prices in other countries. However, the industry appears to corroborate the fact that ability to pay measured through wealth is not systematically used as the criterion for deciding country prices. EFPIA recently published a formal proposal to develop a conceptual framework for equity-based tiered pricing, in order “to ensure that ability to pay across countries is considered in the prices of innovative medicines, anchored in a principle of solidarity between countries, to reduce unavailability of new medicines and access delays” indicating industry awareness of the differences between what countries can afford for novel medicines (11). Therefore, market size and negotiating skills of public counterparts could play an important role in determining industry pricing strategies.

Finally, as with HTA, development of MEA methodologies requires specialized knowledge and skills that could be disproportionately less available in small countries.

Key issues specific to small countries

- Small market size (from the manufacturer’s perspective) and less developed HTA institutions can adversely affect the negotiating power of small countries with pharmaceutical companies, leading to higher prices of novel medicines.
- Development of MEAs that arrange confidential discounts for novel medicines requires specialized knowledge and skills that may be less available in small countries than in large ones, leading to less favourable contractual terms for public payers.

Supply chain issues

Medicine shortages present a growing problem for many European countries. Consequences of shortages include decreased quality of treatment received by patients and an increased burden on health-care professionals, who need to identify and provide alternative treatments. Medicine shortages occur frequently across the WHO European Region – most often involving older, off-patent and generic medicines, such as antibiotics. For instance, in January 2023, the majority of EU countries reported shortages of amoxicillin (21). The causes are multifactorial, with bottlenecks identified along the entire pharmaceutical value chain, from manufacturing of raw materials to national pricing and procurement practices (22).

Besides having fewer products available nationally in the first place, small countries could be further disadvantaged in securing necessary quantities when shortages occur – of both nationally registered medicines and those that need to be imported from other countries – if larger markets are prioritized in absorbing limited stock that is internationally available.

In addition, pharmaceutical companies often require a minimum quantity of stock for purchase, which can be too large for small countries. This means that small countries either purchase more than they need, leading to wastage (especially if they cannot legally come to agreements with the industry to donate doses to other countries) or do not purchase at all, leading to lack of access for patients.

Key issues specific to small countries

- Small countries could be disproportionately affected by shortages of medicines, both because they have fewer products nationally available in the first place and because larger markets are prioritized in absorbing limited stock that is internationally available.
- Pharmaceutical companies often require a minimum quantity of stock for purchase, which can be too large for small countries.

Potential solutions

Potential solutions for these issues, in which WHO can support member countries of the SCI via collaboration or by convening conversations with regional partners, the private sector and other non-State actors through the NMP, including the following.

Joint horizon scanning

Horizon scanning is defined as “systematic identification of health technologies that are new, emerging or becoming obsolete and that have the potential to effect health, health services and/or society” (23). More concretely, it includes identifying new medicines with imminent expected marketing authorization or new uses of existing medicines; estimating and prioritizing their potential impact on patient care, costs, society and the health-care system; and disseminating and updating this information as needed (20). Having a better understanding of what is coming up in the future in the market would allow timely and adequate planning, such that the introduction of these medicines occurs in small countries as well as larger ones without delay.

However, because of the substantial resources required, individual countries are struggling to implement comprehensive horizon scanning programmes on their own. In 2019, only six European countries (Iceland, Italy, Netherlands (Kingdom of the), Norway, Sweden and the United Kingdom) had implemented systematic use of horizon scanning for some new medicines, and four countries (Austria, Denmark, France and Ireland) had some ongoing horizon scanning activities. A recent development is the establishment of cross-country initiatives that aim, among others, to perform horizon scanning jointly. The International Horizon Scanning Initiative (IHSI) initiated by the Beneluxa collaboration is the most advanced undertaking in this respect. Members of the SCI could consider joining IHSI to identify emerging health technologies and their effects on health-care systems and societies. WHO could work with members of the SCI to identify what additional parameters relevant to small countries need to be included in IHSI reports.

Pooled demand and procurement and better collaboration with other countries

Voluntary collaborations, in which several buyers agree to procure medicines exclusively through a procurement group, could be a good solution to reduce the effects of suppliers’ monopolistic status in the case of on-patent medicines by increasing the negotiation power of buyers (24). They might also increase the attractiveness of small countries for producers of essential, older, off-patent medicines and biosimilars, leading to better availability and potentially lower prices. Such voluntary collaborations could be supported by an organisation such as WHO or, where national legislation permits, small countries could undertake joint procurement to gain better access to a wide variety of medicines, ranging from rare generics and biosimilars to orphan drugs and advanced therapy medicinal products. Lessons learned through the Baltic Procurement Initiative between Estonia, Latvia and Lithuania – which was established in 2012 with two primary goals: to reduce public procurement expenditure in the three Baltic countries and to prevent or address supply shortages and thus ensure continuity of access to medicines – would be particularly valuable to these efforts.

Small countries could also link their registration requirements (e.g. the language of packaging and leaflets) to those of larger countries, as this might save generic manufacturer investment costs, thereby encouraging the launch of more generic products. Examples of countries that have already taken steps in this direction include Malta (linked to the United Kingdom), Luxembourg (to Belgium), Monaco (to France), Andorra (to France) and San Marino (to Italy). Exchanges of best practices between these countries and with other countries in the group could also be helpful.

HTA integration

Supporting the establishment and linking up of HTA within the whole medicines and health products life-cycle would support better pricing and ability to negotiate. A network of HTA bodies could help peer learning and sharing of best practices, and could improve transparency. This would also help to build capacity for and mechanisms of handling MEAs, and could be a tool to keep out-of-pocket payments at a minimum and improve sharing across countries on both areas.

The most relevant example of collaboration in HTA is the EU's HTAR, which in the long term will eliminate duplication of effort on the transferable aspects of HTA reports such as data on relative effectiveness and relative clinical safety. Given their constraints in resources required for HTA, member countries of the SCI could consider collaboration – not only in the assessment of relative effectiveness of products (primarily the non-EU countries that will not benefit from HTAR) but also in the non-transferrable aspects of HTA, such as cost-effectiveness analysis and budget impact analysis.

Conclusions

In conclusion, issues and challenges in access to medicines discussed in this policy brief are not strictly specific to the member countries of the SCI, as they are also experienced by other European countries. However, it appears that small countries may be disproportionately affected due to the small sizes of their markets, which make them less attractive for the industry. In addition, dedicating resources and recruiting staff with sufficient expertise in highly technical matters such as horizon scanning, HTA and development of MEAs can be more difficult in small countries, where they may be less available than in larger states. As a result, the most pragmatic strategy to address these issues and challenges is through voluntary collaboration and cooperation, which could be supported by WHO.

Creation of the NMP, a unique multistakeholder platform, was initiated following the conclusion of the Oslo Medicines Initiative. Its aim is to allow Member States, non-State actors and other partners to coordinate, collaborate, prioritize and align efforts to deliver solutions jointly to improve access for patients. Governance of the NMP is by the Standing Committee of the Regional Committee, with the WHO Regional Office for Europe hosting the secretariat. Sustained collaboration between all entities is needed to agree, co-develop and implement a comprehensive set of actions in accordance with WHO's framework of engagement with non-State actors and other relevant WHO procedures. As a multistakeholder platform, the NMP is uniquely placed to provide a space for member countries of the SCI to work with each other and with non-State actors, including industry and other partners, jointly to ensure equitable access for all patients in need, and to safeguard the sustainability of health-care systems and the innovation of medicines. The work of the NMP will also facilitate consideration of the lifecycle of medicines and improved access to generics and biosimilars.

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The WHO Regional Office for Europe

The World Health Organization (WHO) is a specialized agency of the United Nations created in 1948 with the primary responsibility for international health matters and public health. The WHO Regional Office for Europe is one of six regional offices throughout the world, each with its own programme geared to the particular health conditions of the countries it serves.

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