Health and Youth Care Inspectorate
Ministry of Health, Welfare and Sport

Inspections in the field of medicines, blood and tissues

by the Health and Youth Care Inspectorate of the Netherlands

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INSPECTIONS IN THE FIELD OF MEDICINES, BLOOD AND TISSUES

In the Netherlands, the Health and Youth Care Inspectorate (HYCI) is the supervisory authority for the quality, safety and availability of medicines and blood and tissues for human use[1]. Within the HYCI, the Department of Pharmaceutical Products monitors the entire chain from (pre)clinical investigations to production, transport and, finally, the safe application of medicines following their market authorisation.

Area of work

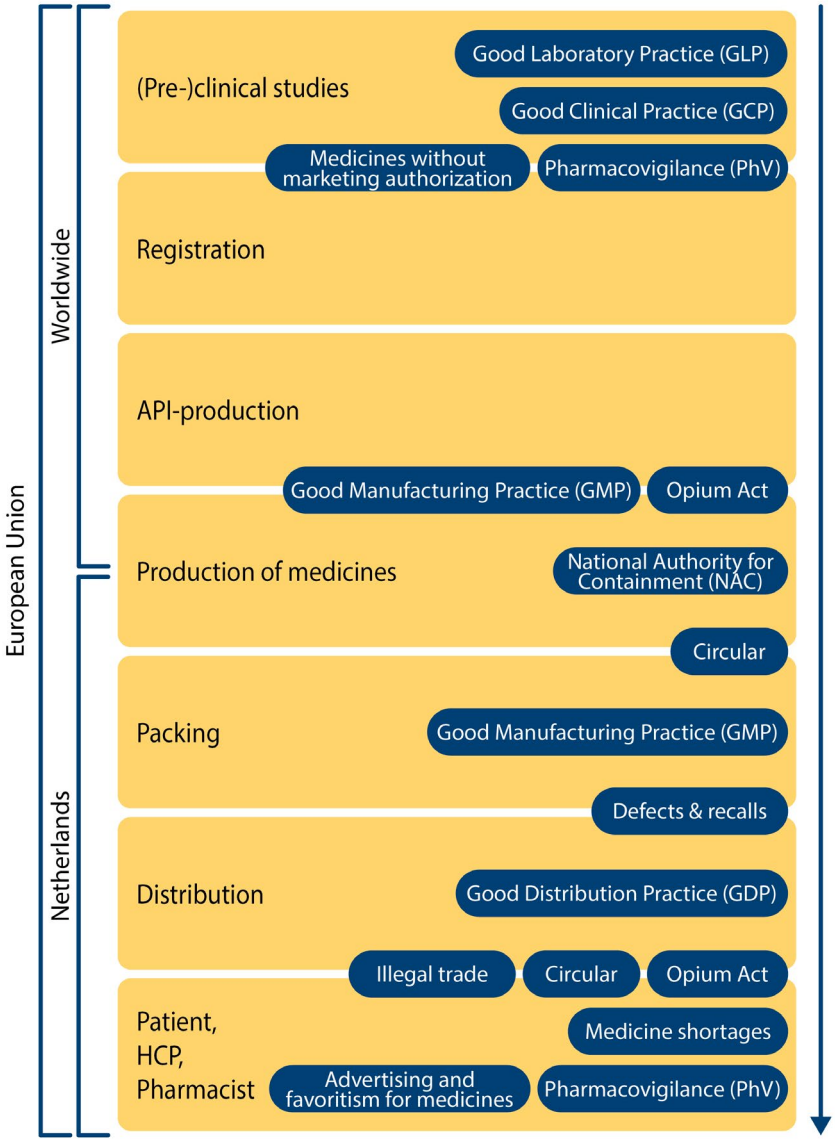
In the Department of Pharmaceutical Products we assess whether companies comply with a variety of laws, regulations and norms. Our teams are engaged with a wide area of work: from manufacturers and distributors to clinical trials; from organ donation, blood and tissues to categorised drugs and medicines without marketing authorisation; from promotions to illegal trade.

Alerts, inspections and assessments

Each year we receive about 800 safety alerts for medicines and our inspectors conduct about 600 visits in the Netherlands and abroad. In addition, we assess some 220 applications for a new or amended licence. We grant and monitor exemptions for the use and handling of drugs listed in the Dutch Opioid Act for public health or research applications. And we regularly give presentations about our work and expertise for pharmaceutical companies and pharmacists.

1 Where we write 'medicines', we also mean to include active pharmaceutical ingredients (APIs), investigational medicinal products (IMPs) and substances of human origin

Simplified representation of the various areas of expertise in the chain of pharmaceutical products:



Supply of unregistered medicines by a Doctor's Declaration and medicine shortages

Every year we receive about 2,000 applications for supplying medicines without marketing authorisation upon request by a Doctor's Declaration. This concerns a medicine that is not registered in the Netherlands, but is essential for the treatment of a patient. Each year the number of applications increases and about 40% is an urgent request, meaning that a decision is needed within one to five days.

Together with the Medicines Evaluation Board (MEB) we host the Medicine Shortages and Defects Notification Centre. In the case of a medicine shortage, the HYCI can decide that a similar product may be procured from abroad by issuing a Shortage Resolution. We issue about 140 of these resolutions annually. Furthermore, we work closely together with multiple stakeholders in order to prevent shortages or to decrease negative effects on patients.

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Determination of Product Classification

We offer advice on the status of products, both end products and active substances. In short, we determine whether a product is a medicine or another type of product. Each year we perform such determinations for about 150 products upon request by our partners. These include the Dutch Customs, the Netherlands Food and Consumer Product Safety Organisation (NVWA), the Fiscal Information and Investigation Service (FIOD), the Police or the Public Prosecutor's Office.

In this effort we closely collaborate with our colleagues from the National Institute for Public Health and the Environment (RIVM) in case a laboratory investigation is necessary. Together with the NVWA we host the national Advisory Board for the Determination of Product Classification.

NATIONAL INSPECTIONS

The Department of Pharmaceutical Products monitors the entire chain of medicines. To this end, we collaborate with various parties.

Collaborations

We work closely together with other government bodies within the Ministry of Health, Welfare and Sport (VWS). We also have close ties with the Directorate of Medicines and Medical Technology and with the Medicines Evaluation Board (MEB). Together, we work on matters such as the supply of medicines, shortages, illegal trade and magistral or pharmacy preparations of prescription drugs.

Furthermore, we collaborate on revising European guidelines for medicinal products and its consequences for our inspections. In addition, we regularly align with the Directorate of Public Health on medical and scientific research on humans and with the Directorate of Food, Health Protection and Prevention.

There are many more government parties with whom we collaborate, as well as branch organisations in the field. Some of these are listed in Table 1.

Table 1

Government parties	*Umbrella organizations*
- the Central Committee on Research Involving Human Subjects (CCMO) together in the supervision of the Medical Scientific Research Act (WMO); - Netherlands pharmacovigilance centre Lareb in the supervision of pharmacovigilance; - the Customs and the Public Prosecution Service (OM) to prevent the illegal trade of medicines and active substances; - the National Institute for Public Health and the Environment (RIVM) regularly carries out laboratory research for the Health and Youth Care Inspectorate (IGJ); - We consult with Ministry of Health, Welfare and Sport and the Dutch Healthcare Authority (NZa) for the post-mortem tissue chain; - Other supervisors such as the Netherlands Food and Consumer Product Safety Authority (NVWA).	- Royal Dutch Society for the Advancement of Pharmacy (KNMP); - Dutch Association of Hospital Pharmacists (NVZA); - Dutch Federation of University Medical Centers (NFU); - Association of Innovative Medicines (VIG); - Biosimilars and Generic Medicines Industry Netherlands (BOGIN); - BG Pharma; - Pharmacovigilance Platform Netherlands (PPN); - the Foundation Code of Medicines Advertising (CGR); - The foundations Inspection Council for Public Promotion of Medicines (KOAG); - Inspection Council for Promotion of Health Products (KAG); - the industry parties in the Pharmaceutical Technical Consultation Industry (FTOI).

Because of the complexity of the Dutch pharmaceutical landscape we partake in many (multidisciplinary) meetings on both an operational, strategic and government level. In the end, we keep an eye on the impact of (new) legislation from both a substantive and a pragmatic perspective.

Pandemic preparedness

Pandemic preparedness has got societal and political attention on both a national and international level.

In a European health crisis EMA is responsible for coordinating the reactions of the European Member States in the case of a shortage of critical medicines.

During the COVID-pandemic the importance of clear communication became evident. This is why we scrutinise sources of false information or unauthorised advertising for medicines.

Illegal supply and trade

Everyone in the Netherlands must be able to trust that medicines are genuine and of good quality. We notice that the illegal supply of medicines and active substances is increasing. This trend puts the public trust under pressure and sometimes causes serious medical risks.

This is why we are committed to counter illegal supply and illegal trade in medicines and active substances. We do this by making the public aware of the health risks associated with buying from unregulated websites (when there is no demand, there will be less supply) and by actively having websites and/or advertisements taken down. To this end, we collaborate with online sales platforms, such as Marktplaats (a Dutch trading platform). Furthermore, we take action by imposing fines and by confiscating illegal medicines. Where necessary, we engage the Police or the Public Prosecutor's Office.

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INTERNATIONAL INSPECTIONS

International developments, European legislation and international trade relations have a direct impact on our inspection activities.

The development, production and (quality) control of medicines takes place at various locations worldwide. Many of these locations are outside the European Union.

In the Netherlands we import materials to be processed into medicines. For example, from China and India, but also from the United States and Canada. Because of the advantageous presence of Schiphol Amsterdam Airport, the port of Rotterdam, the location of EMA in Amsterdam and the favourable Dutch financial climate, many companies choose the Netherlands for their headquarters.

Collaboration

Dutch laws and regulations for pharmaceutical products and substances of human origin are mainly determined by the laws imposed by the European Union. Inspections in third countries are distributed amongst the various national inspectorates of European Member States. A smooth international cooperation is therefore key in our inspection activities.

Our inspectorate collaborates closely with EMA and the European Directorate for the Quality of Medicines (EDQM). We play an active role in various EMA committees and working groups. We also take part in the Pharmaceutical Inspection Co-operation Scheme (PICS) and in various meetings of the Heads of Medicines Agencies (HMA). We do this to align the activities of inspectors within the European Union and also to discuss strategic themes, such as capacity building and training.

Though being an Inspectorate ourselves, we also accommodate audits of our own inspection work. These audits typically have an international

context, and they involve the Union Control by the European Committee for Clinical Investigations - GCP, the Joint Audit Programme (JAP) of the EMA and the On-Site Evaluation (OSE) for GLP from the OECD.

Also, illegal supply and trade do not stop at national borders. This requires an international approach. Collaborating with national and international partners is therefore crucial. Our inspectorate takes part in the Working Group of Enforcement Officers (WGEO) and we are involved in various international efforts, such as Operation Pangea to disrupt the online sale of counterfeit and illicit health products.

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FOCUS ON THE FUTURE

We work in a dynamic pharmaceutical landscape. Ever changing laws and regulations and adaptations in policy, a growing number of production facilities within the European Union and alterations in supply chains have our continuous attention. We also observe more and more complex and innovative products, various types of product defects and an increase in illegal trade. Our challenge is to maintain focus. We focus our attention on the quality, safety and availability of medicines. In this effort we make our decisions largely based on the risks that we find in our inspection work.

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We centre our focus on three themes:

1. To have an international strategic impact

We are adamant to maintain our good relation with the Ministry of Health, Welfare and Sport and the Medicines Evaluation Board and to establish a strong international position together. In this way, we can be involved in and provide our input in the making of (inter)national legislation. In addition, we work with MEB and EMA to ensure an internationally even burden in inspection activities.

2. To collaborate optimally on a national level

We are committed to making clear agreements with other parties on the division of labour. In this way, responsibilities are clear when areas of work overlap. We are also working on a complete stakeholder analysis.

3. Inspections with impact

We are performing a comprehensive analysis to determine where risks and opportunities lie, using online and offline data. We use our findings to organise our supervisory activities. In the end, we feel a responsibility to be there where the biggest risks are and where our actions have the most profound impact.

By discussing our supervisory tasks with other supervisory authorities we can add to and support each other's activities. This helps us in focussing our activities, where they are needed the most.

In addition to conducting mandatory inspections we are working more and more towards risk-based inspections. This will increasingly allow us to deal with current topics in society.