LÆGEMIDDELSTYRELSEN
DANISH MEDICINES AGENCY

2025

Danish Medicines Agency

Annual OMCL Report 2024

Lægemiddelstyrelsen / Danish Medicines Agency
Axel Heides Gade 1
2300 Copenhagen S
Denmark
lmst.dk

Annual OMCL Report 2024
Medicine control, OMCL network, Analytical results

Language
English

Version
1.0

Version date
June 2025

Distributed by
Lægemiddelstyrelsen / Danish Medicines Agency
10.06.2025

ISBN
978-87-92390-56-1

Table of contents

1 Organisation of the Danish OMCL 4
1.1 General structure of the Danish Medicines Agency 4
1.1.1 Department of Control and Security of Supply 6
1.2 Personnel Matters of the Danish OMCL 7
1.3 Quality management system 8
1.4 Internal collaboration 9

2 Activities related to the national market 10
2.1 Legal Supply Chain (authorised medicines) 10
2.1.1 Sampling approach 10
2.1.2 Results 10
2.1.3 Details/technical issues 13
2.2 Legal Supply Chain (medical devices) 13
2.2.1 Sampling approach 14
2.2.2 Results, details/technical issues 14
2.3 Legal Supply Chain (suspected samples) 14
2.4 Illegal Supply Chain 14

3 Activities related to the network 15
3.1 Proficiency Testing Studies 15
3.2 Radiopharmaceutical Laboratory 15
3.3 Chemical Laboratory 16
Biological Laboratory 19
3.4 General Regulatory Tasks 19

4 Method related activities 22

5 Public relation activities 22

6 Future planning 24
6.1 National 24
6.2 Network 24

7 Difficulties encountered 25

1
Organisation of the Danish OMCL

This section provides a short description of the Danish Medicines Agency, the Danish Official Medicines Control Laboratory (OMCL) and its staff, our quality management system and status of accreditation.

1.1 General structure of the Danish Medicines Agency

The Danish Medicines Agency has around 650 employees, and the four largest professional groups in our organisation are pharmacists, administrative assistants, doctors, lawyers and masters of social science (organizational chart next page, Figure 1). The Agency perform most of the tasks in close collaboration with colleagues from regulatory authorities and organizations in the other EU countries.

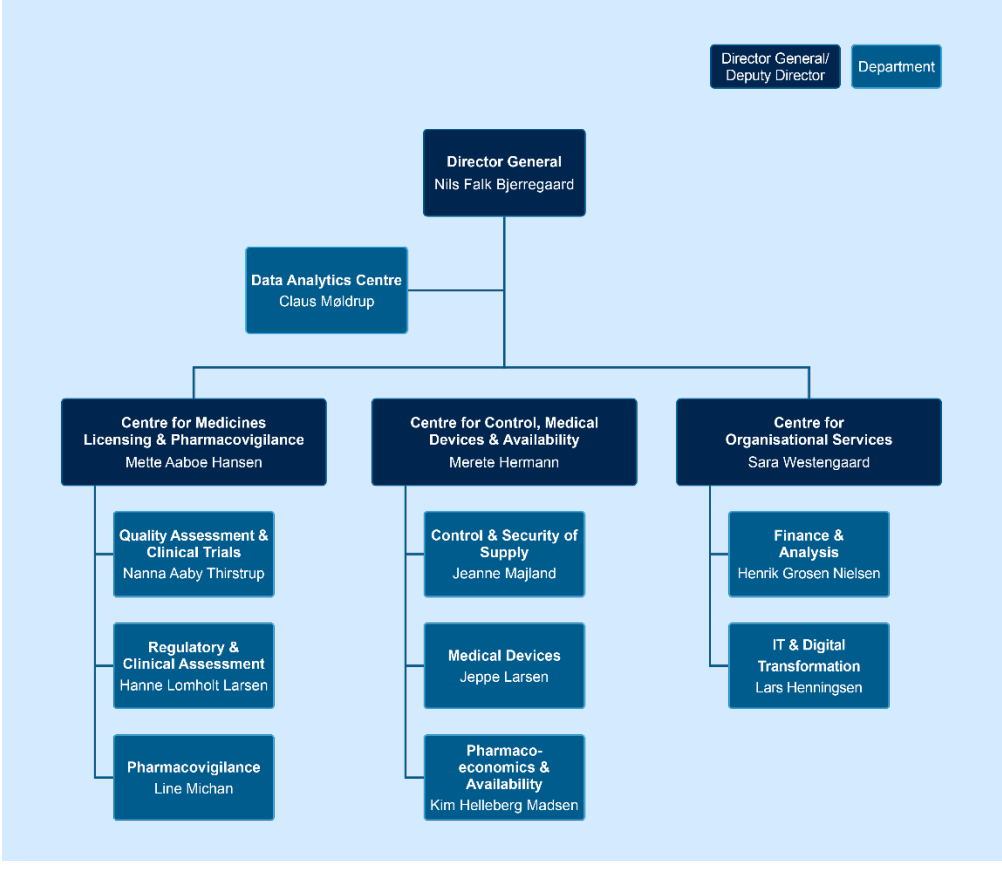
The Danish Medicines Agency

- authorises and inspects pharmaceutical companies and licenses medicinal products in the Danish market
- monitors adverse reactions from medicinal products
- authorises clinical trials
- decides which medicines are eligible for reimbursement
- monitors medical devices available in Denmark and supervises adverse incidents involving medical devices
- appoints proprietary pharmacists, organises the pharmacy structure and supervises pharmacies and retailers.

The Danish Medicines Agency mission, vision and strategy 2022-2026 is described at the webpage together with the statements that we live by

- The Danish Medicines Agency mission, vision and strategy 2022 - 2026

FIGURE 1
ORGANISATIONAL CHART OF THE DANISH MEDICINES AGENCY



Source: Organisation (November 2024)

New Director General of the Danish Medicines Agency

In 2024 the Danish Medicines Agency had a new director. The Danish Ministry of the Interior and Health appointed Medical Director Nils Falk Bjerregaard as Director General of the Danish Medicines Agency as of 1 November 2024.

Nils Falk Bjerregaard holds an MSc in Medicine from Aarhus University (2002) and became a medical specialist in anaesthesiology in 2009. He brings extensive and diverse management experience from many years in the hospital sector.

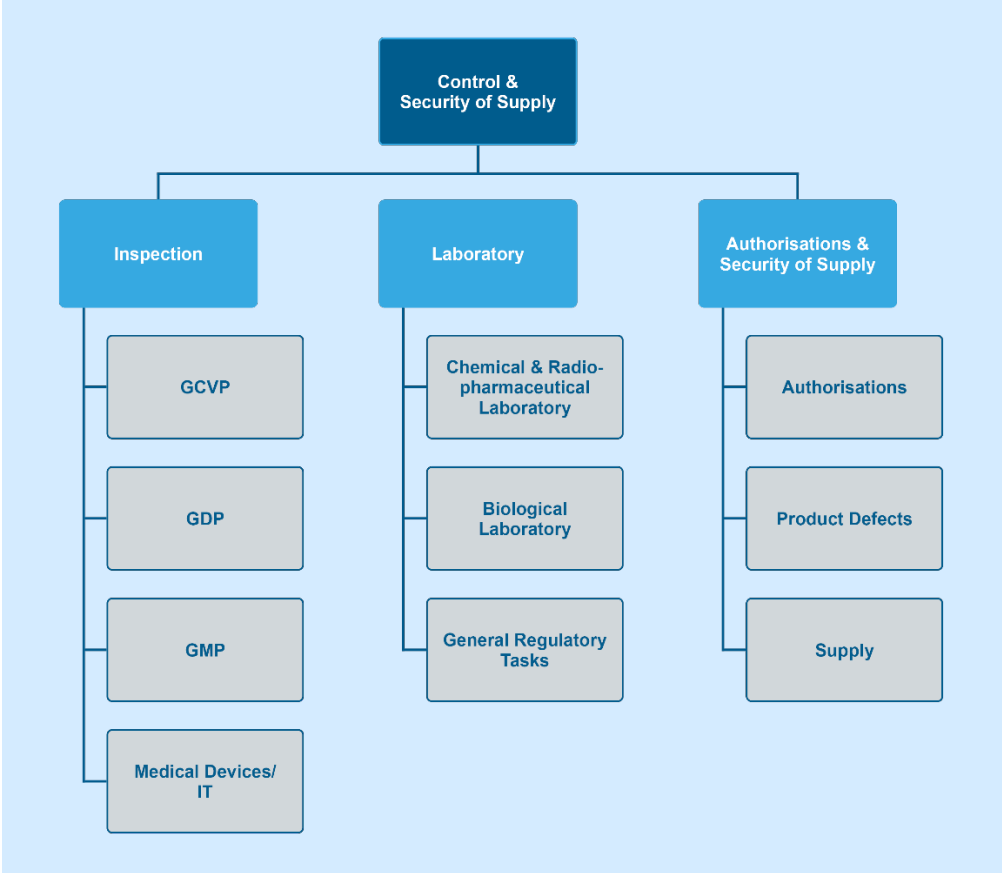
Since 2018, Mr Bjerregaard had been Medical Director at Horsens Regional Hospital and, as part of the Group Management in the Central Denmark Region, he had gained valuable experience from a knowledge-intensive and operationally demanding organisation characterised by a high degree of interdisciplinarity.

1.1.1 Department of Control and Security of Supply

The department “Control and Security of Supply” is responsible for the Danish Medicines Agency's regulatory duties with respect to laboratory testing and monitoring of medicinal products. The Danish inspectorate is located in this department of the Danish Medicines Agency. The Unit “Authorisations & Security of Supply” handles complaints and reports about quality defects in medicinal products as well as any related recalls. This Unit also supervises company authorizations for handling and manufacturing medicinal products and monitor the supply of medicinal products.

The laboratory Unit contains the Danish OMCL. In addition to OMCL activities, the laboratory performs tasks in connection with the elaboration, testing and perform verification of monographs for Ph. Eur. The National Pharmacopoeia secretariat is also placed in the Laboratory.

FIGURE 2
ORGANISATIONEL CHART OF THE DEPARTMENT OF CONTROL & SECURITY OF SUPPLY



Laboratory: The Danish Official Medicines Control Laboratory (OMCL)
GCVP: Good Clinical & Vigilance Practice
GDP: Good Distribution Practice
GMP: Good Manufacturing Practice

A separate Annual Report on OCABR activities is provided.

Risk-based model for the selection of new kontrol projects
When taking a medicinal product in for a control it is not possible to check every control point every time for all products controlled. This is a consequence of the complexity and the number of control points.

For selection of new control projects for medicinal products and active substances for testing, the Danish OMCL has developed a risk-based model based on OMCL documents including "Incorporation of a risk based approach in Market Surveillance testing at OMCLs, PA/PH/OMCL (06) 3 R11" and inputs from other countries. Consequently, the OMCL have worked extensively to revise the risk model together with the Agency's computational resources at DAC (Data Analytics Centre).

The Danish OMCL are now utilizing a risk model database which has defined many different risk parameters based on available electronic data sources. These parameters are such as time elapsed since last control, consumption, complaints from patients as well as medical professionals, and findings during previous controls and inspections. The different risk parameters have been ranked, and therefore the risk model database gives an automatic risk scoring. Moreover, we carry out risk-based control adjusted to the individual situation. Therefore, from this risk model database, different projects are extracted depending on the scope for example elderly products, formulation as vaginal products. The result is an updated list of prioritized medicines selected for control of products for the next three years.

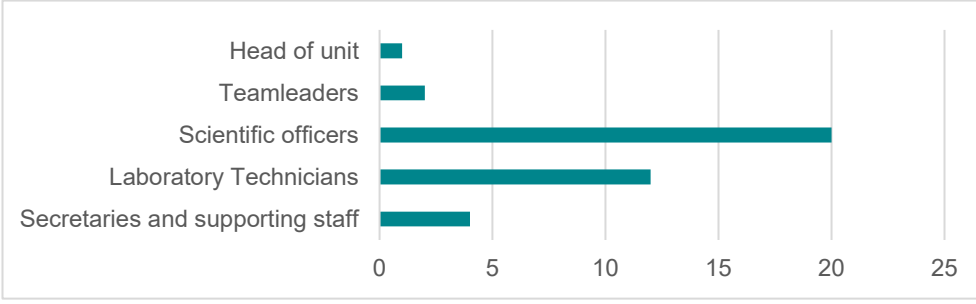
Meanwhile an agreement with DAC is maintained to upgrade the data sources on a regular basis. Furthermore, the risk models must be dynamic in order to prevent the model from becoming predictable, therefore after evaluation in 2024 it is time to update the risk model so a new list of prioritized medicines can be in place ultimo 2025.

The OMCL have in 2024 been promoting the Danish model outside the borders of EU and therefore Brazil and Mexico have been learning about the Danish risk-based model and how to build up their own risk model based on available material in their countries. These visits also gave us the opportunity to introduce the work from the HMA Drafting Group for Risk-based Approach to Product Testing. The HMA pre-authorisation risk assessment model has become compulsory as of March 2020 for all new MRP and DCP product registrations.

1.2 Personnel Matters of the Danish OMCL

The Danish OMCL was in 2024 divided in the tree teams: Chemical and Radiopharmaceutical Laboratory, Biological Laboratory and General Regulatory Tasks. In total, the Laboratory had 39 employees. The staff distribution according to role is presented in Table 1.

TABLE 1
2024 STAFF DISTRIBUTION BASED ON ROLES AT THE DANISH OMCL



1.3 Quality management system

Since 1995, the Danish OMCL has been accredited according to the requirements of ISO 17025 and has been subject to a regular independent surveillance programme. In 2006, the accreditation included a flexible scope accreditation. The accreditation of the Danish OMCL was renewed in April 2022.

The scope of the accreditation is testing of pharmaceutical products and active ingredients and is linked to a specific list of methods mainly from Ph. Eur. and list of methods/techniques authorized by the accreditation board.

Our national accreditation body for the Danish OMCL is DANAK.

Types of testing:

- **Biological and biochemical**
- **Chemical testing**
- **Radiochemistry and radiation**

The Danish OMCL received the first MJA attestation on February 2011. The specified field of activity for the OMCL is “Testing of pharmaceutical products and API (biological, chemical and radiopharmaceutical); Market surveillance testing and screening for illegal products; Elaboration of standards and reference materials to Ph. Eur.; Participation in PTS, CAP, BSP, CRS and MSS”. The most recent MJA in 2023 was successfully carried out as a joint audit with DANAK. The Danish OMCL participated in the JAP (Joint Audit Programme) audit of the GMP inspectorate of the Danish Medicines Agency in September 2024.

BEMA (Benchmarking of Medicines Agencies) in November 2024 was successfully carried out for the Danish Medicines Agency. The OMCL contributed with documentation for the self-evaluation.

Work is ongoing with focus on evaluation of measurement uncertainty, data security and computerised systems.

1.4 Internal collaboration

The GXP-inspectors, quality assessors and OMCL are located in the same organization and geographical location. GXP inspectors and OMCL are organized in the same department and building. The quality assessors, GMP/GDP inspectors and OMCL staff have access to the same databases and all data are available to enable quality assessors to make decisions on the acceptability of manufacturers nominated on applications for marketing authorisations as well as post-marketing control. The inspectors are obliged to update the common database after inspections including the inspection result as a score, and for GMP inspections, the information about issued GMP certificate. The quality assessors and OMCL staff have access to the same database. Information on conducted lab controls on specific medicinal products are shown in the same database via a link to the ECM-system. Marketing authorisations are included and linked to data on company authorisations and inspections.

Competence teams – a number of multidisciplinary teams have been set up across the Agency, which cover topics including grey zone products with blood, cells and tissues, pharmacovigilance, parallel imports and radiopharmaceuticals. All members contribute with relevant subject for discussion during the meetings and risks can be identified and handled accordingly.

Triggered inspections can be requested by assessor/OMCLs and other stakeholders. Scientific officers from OMCL, Licensing, Clinical trials and others, have a standing invitation to participate in all types of inspections, and are sometimes requested formally because of special circumstances. Inspectors can sample during inspections and bring samples to the OMCL for testing. If decided before the inspection details on the sampling are agreed in advance.

Hand over meetings between inspectors and OMCL staff/quality assessors are planned when needed (to make the understanding between inspectors and assessors better). A yearly meeting before finalizing the OMCL activity is usually planned.

The collaboration between quality assessors, inspectors and OMCL, is formalized and the advantage of being under the same roof is of huge importance; the inspector can go to the assessors/OMCL and discus any issue with the chemists, as well as the opposite way.

Also located in the department is the unit “Authorisations and Security of Supply” who handles complaints and reports about quality defects in medicinal products as well as any related recalls. When any systematic defects are detected they can inform the OMCL or the Inspectors to trigger a test or an inspection.

2
Activities related to the national market

This section gives an overview of the Danish OMCL sampling approach, results of testing and workload on both the legal and illegal supply chain to the Danish market.

2.1 Legal Supply Chain (authorised medicines)

The Danish OMCL carries out analyses on a range of medicinal products both according to the authorized dossier of the marketing authorization holder (MAH) as well as in-house (validated and non-validated) methods. In general, selected testing which typically includes appearance, physical tests such as uniformity of mass and hardness, assay of active ingredient(s) and impurities is performed.

Furthermore, the OMCL performs supplementary tests for specific products or drug substances. Where possible investigations review the labelling and the documentation such as batch protocol, certificate of analysis (CoA) and/or specification compliance. Some investigations only review the labelling and/or documentation without the typical analysis performed in the laboratory.

2.1.1 Sampling approach

As mentioned in 1.1.1 the Danish OMCL use a risk-based model for the process of selecting medicines for control. This risk-based model utilizes powerful computational resources to include several parameters, such as time elapsed since last control, novelty, complaints from patients as well as medical professionals, and findings during previous controls. Liaising with DAC, has enabled the Danish OMCL to establish updated lists of prioritized medicines or groups of medicines for control.

2.1.2 Results

As described in 2.1 for every control one or various tests are conducted on the finished product, API or illegal substance. The workload for each product has increased as the analyses get more complex and more tests are conducted per product than previous years. For some products multiple bathes are controlled when relevant for the control project.

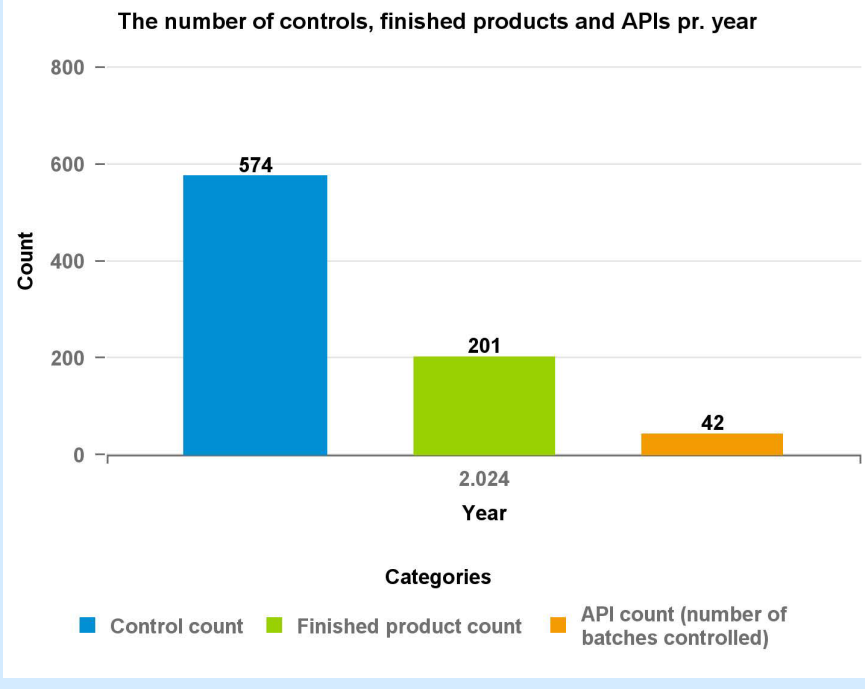
For most finished products more than one type of control (laboratory analysis, documentation review, labelling control) was performed and some finished products and API's had multiple batch numbers investigated. For products where more than 3 controls or laboratory analyses are performed a complexity factor are added to give the control count.

The workload of the Danish OMCL is best described by the control count which in 2024 was 574. The key performance indicator (KPI) for the control count is 350.

A total count of 201 different finished products were called in for control in 2024. The KPI's for the number of finished products is 150 different products.

The statistics for the work performed in the Danish OMCL for 2024 are shown in figure 3.

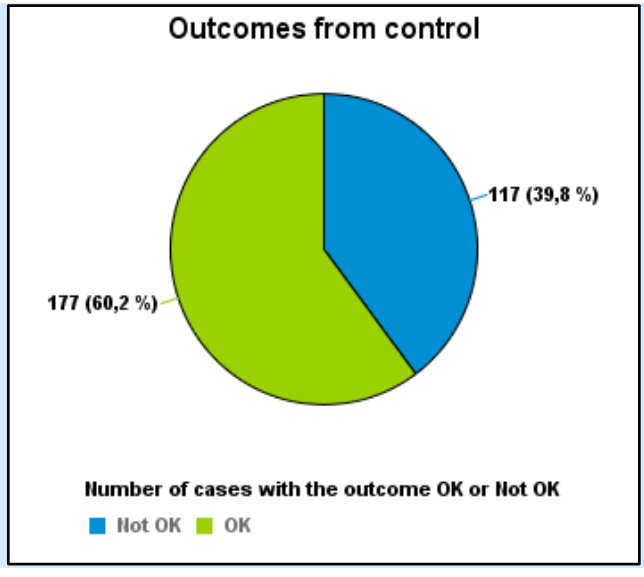
FIGURE 3
OVERVIEW OF THE WORKLOAD FOR THE DANISH OMCL IN 2024



Source: SAB BI report (modified) "OMCL Årsrapport", "Figur, pr år"
Data extracted: 20250409

The outcome distribution of the laboratory control is shown in figure 4. As mentioned each control may cover more than one test. In this figure the worst outcome of the tests performed for each control is reported. The outcome is divided in OK (all tests complies) and Not OK (minimum one test does not comply = lead to remarks, enforcement notices or evaluation of recalls).

FIGURE 4
OVERVIEW OF THE CONTROL RESULTS IN 2024

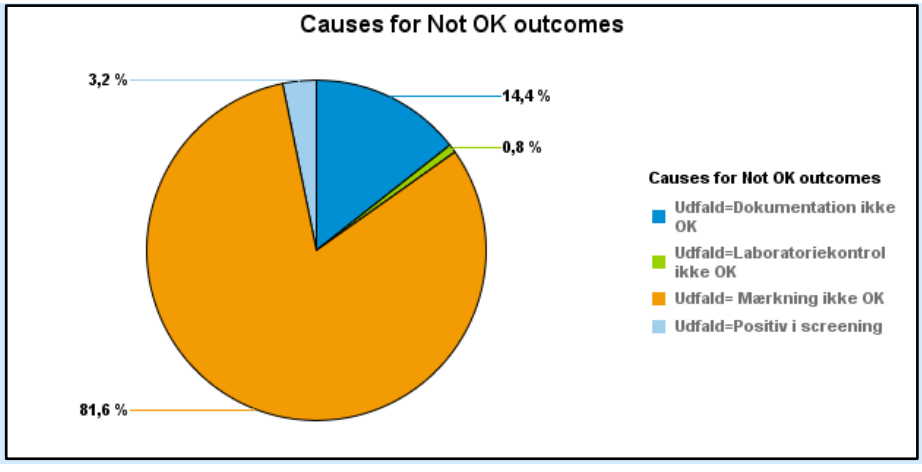


Source: SAB BI report ”OMCL Årsrapport”, “Diagram of outcomes”
Data extracted: 20250220

If the case outcome results in an evaluation of recall, the case will be forwarded to the unit of Authorisations & Security of Supply for further evaluation. The evaluation of the need for a re-call includes an assessment of the non-compliance considering the security of supply to the Danish marked.

Of the 39.8 % controls in 2024 which were “Not OK” most of the noncompliance were related to labelling comments. The second most common cause of noncompliance related to comments to the documentation. Very few noncompliance related to the laboratory analyses. The distribution of causes for noncompliance for 2024 is shown in figure 5. The distribution of noncompliance does not vary significant from former years.

FIGURE 5
OVERVIEW OF THE TYPES OF NONCOMPLIANCE DETECTED IN 2024



Source: SAB BI report ”OMCL Årsrapport”, “Diagram of outcomes”
Data extracted: 20250220

Explanatory note:
Udfald=Dokumentation ikke OK = Documentation review was not in compliance
Udfald=Laboratoriekontrol ikke OK = Laboratory analysis was not in compliance
Udfald=Mærkning ikke OK = Labelling was not in compliance
Udfald=Positiv I screening = Positive hit in the screening of suspected illegal samples

2.1.3 Details/technical issues

For a list of the finished products analysed by the Danish OMCL see “*2024 OMCL Annual Report Annex 1”*. This annex will not be published on the website of the Danish Medicines Agency for public consultation. Any findings have been discussed with and are corrected by the MAH.

2.2 Legal Supply Chain (medical devices)

The control of medical devices on the Danish marked is not in the scope of the Danish OMCL. The market surveillance and user safety are managed by the department for Medical Devices within the Danish Medicines Agency.

2.2.1 Sampling approach

Healthcare professionals, manufacturers, distributors and importers of medical devices have a duty to report to the Danish Medicines Agency if a device results in an accident or incident regardless of whether the cause is a device malfunction or misuse. Citizens can also submit reports.

2.2.2 Results, details/technical issues

No testing of medical devises was performed by the Danish OMCL in 2024.

2.3 Legal Supply Chain (suspected samples)

The Danish Medicines Agency did not carry out any analysis on counterfeit medicines during 2024 (see Table 2).

2.4 Illegal Supply Chain

The Danish OMCL laboratory continues to analyse products suspected of containing undeclared APIs. However, the number of products received at the laboratory has fallen considerably in the last few years. Samples are primarily analysed by liquid chromatography coupled to a high-resolution mass spectrometer (LC-HRMS). The products are usually in the form of either tablets or capsules. However, the OMCL also receives samples of powder.

In 2024, six products were tested at the OMCL. Four of the products were found to contain undeclared active pharmaceutical ingredients.

The number of samples analysed by the Danish OMCL is presented in Table 2.

TABLE 2
TOTAL NUMBER OF SUSPECTED COUNTERFEIT SAMPLES TESTED FROM THE LEGAL AND ILLEGAL SUPPLY CHAIN

		2024
Total number of suspected counterfeit samples in the legal supply chain	a	0
Total number of confirmed counterfeit samples of licensed medicines in the legal supply chain	b	0
Total number of suspected illegal samples tested	g	6
Total number of illegal samples identified (other than counterfeit samples in the legal supply chain - b)	c+d+e+f	unknown

Case outcome applicable for *g* is available in "*2024 OMCL Annual Report Annex 1"*. This annex will not be published at the Danish Medicines Agency website.

3
Activities related to the network

In this section some of the highlights from the OMCL's activities related to the network is reported.

3.1 Proficiency Testing Studies

For the purpose of quality assurance, the Danish OMCL have analysed the following PTS-samples in 2024: PTS238, PTS239, PTS245, PTS247 and PTS248.

A few of the PTS's were analysed by all tree laboratory teams (Chemical, Radiopharmaceutical and Biology).

The biological laboratory also participated in the Collaborative Study for the Prekallikrein standard BSP167. Furthermore, PTS PH088 for Subvisible particles (Ph. Eur. 2,9,19) from another provider were performed.

Also, the Radiopharmaceutical laboratory finished the PTS NPL for the Radioactivity Proficiency Test Exercise 2023.

All PTS results was considered satisfactory.

The Danish OMCL participated in the SUP013 (Analysis of Suspicious Unknown Products). The OMCL successfully identified the substance in the tablets as melatonin and, as such, the result was considered satisfactory.

3.2 Radiopharmaceutical Laboratory

The Danish OMCL has performed analytical control of selected radiopharmaceuticals. The analytical control was initiated by different channels as, revised Ph Eur monograph, requests from another OMCL and our in-house risk-based testing plan with focus on radiopharmaceuticals using Technetium-99m. The control included medicinal products with the formulation *kits for radiopharmaceutical preparation* as well as the *radionuclide generator* with focus on determination of radiochemical purity and/or radionuclide purity.

To ensure the quality of the prepared kit it is important that the Technetium-99m labelling procedure (kit preparation procedure) used by the MAH is equivalent to the procedure available for the hospitals, described in the SPC. Therefore, the agreement of these procedures was a focus point in our control as well.

The stated activity ranges for the Technetium-99m labelling procedure was also tested during the laboratory control.

As the Danish OMCL is the only laboratory with facilities and competences in testing of radiopharmaceuticals within the network of Official Medicines Control Laboratories (OMCL), details and outcome of all control performed on radiopharmaceuticals independent on licensing procedure are exchanged within the network in the specific folder 'Document Upload' in the MRP/DCP database.

3.3 Chemical Laboratory

Participation in marked surveillance studies (MSS)
In 2024 the Danish OMCL participated in two Market Surveillance Studies (MSS studies), which were initiated and coordinated by the EDQM.

MSS063 Rosuvastatin

The Danish OMCL participated in the MSS063 Rosuvastatin Tablets and API, where 29 finished products and 21 APIs were analyzed for Identification, Assay, Related substances, Impurities (only APIs), Water content (APIs only) and Dissolution (Finished products only). All samples complied with the specification limits, and all results were reported to EDQM.

As all products were collected directly from the MAH, the MSS was combined with the sampling of API for a parallel project on Residual solvent. The extra received API's were analyzed according to our In-House Residual Solvent method. All API samples complied.

MSS062 Pregabalin

In the MSS062 Pregabalin Hard Tablets, 44 finished products from the Danish marked were required. Samples came from 8 different MAH and 3 parallel import companies. The tests performed for the products where appearance, identification, mass variation, content uniformity and assay. For the highest dosage, 10 samples, the analysis for the related substances were also performed. For all products a full labeling control where performed. Comments on corrections to the labeling where given to 1 parallel importer and 4 MAH, of which 3 of them where send to a different department in the Danish medicine agency for further handling. Corrections where about font size for readability, unreadable lot and expire date on inner packaging and inadequate anti-tampering devise. This will be corrected by the MAH/parallel distributer.

MRP/DCP collaboration
For the MRP/DCP collaboration and mutual agreement on testing medicinal products the Danish OMCL send 11 finished products for analytical tests at another OMCL.

When MRP/DCP approved medicinal products are sampled from the Danish marked, an extra sample is requested for the labelling check in order to perform the labelling check in parallel with the analytical test.

Verification of Ph. Eur. Draft monographs
Metronidazole benzoate

The monograph for Metronidazole benzoate (0934) has been updated with a specification for unspecified impurities of maximum 0.05% and a changed reporting threshold to 0.03%, since the maximum daily dose of this API can be above 2 g and therefore were not complying with ICH Q3A. The Danish OMCL performed a verification of the related substances method which included stability of solutions, accuracy, linearity, repeatability, symmetry factor and LOD/LOQ calculation of both the API and the specified impurities A, B and C. Furthermore, batch control was performed of six elder batches.

The verification showed that all results were acceptable. This work has been reported to the EDQM. Afterwards our report was sent to the expert group and used for the publication of the updated monograph of Metronidazole benzoate which were publicated in the Pharmaeuropa 36.2.

National market surveillance studies
A number of different control projects were performed on the national marked.

Complaint: Visual change of appearance and effect

In 2024 the Danish OMCL were contacted by a private citizen representing a Facebook group, who wrote regarding concerns that their medication had changed. Over all, they all experienced various changes in the effect and the physical look of the medication. The MAH were involved in the complaint. In total 9 different samples covering batches released in different years, were tested by the OMCL.

All samples were analyzed for Assay, disintegration, mass variation and pH. All samples complied with the specifications, and no differences between the samples were detected. The MAH did not find any deviations during the product and release of the tested samples, and the samples the Facebook group shared information about. No further actions were initiated.

Disintegration test for solid rectal and vaginal dosage forms

The project aimed to test the disintegration of vaginal and rectal preparations (suppositories, vaginal capsules and vaginal tablets) according to to Ph.Eur. 2.9.2 Disintegration test for solid rectal and vaginal dosage forms, and also to use new equipment and maintain testing experience.

13 vaginal/rectal preparations from 8 MAH's were analyzed. Full labeling control and partial documentation control were also carried out.

All products complied to the requirements for disintegration. There were comments to the labelling for 5 products and to the documentation for 5 products.

One product (a suppository) was authorized according to Ph.Eur. 2.9.1 Disintegration of tablets and capsules. The product was tested according to Ph.Eur. 2.9.2, of which the requirements were fulfilled. The MAH was recommended to change the analysis method for disintegration in the finished product specification from Ph.Eur. 2.9.1 to Ph.Eur. 2.9.2.

Stockpiled medicine; Potassium Iodide

A stability test of the emergency storage of Potassium iodide tablets in Denmark were performed. The test concerned analysis on 9 random batches. All samples complied with the specification limits. Results were reported to the Danish Health authority (SST).

Risk based projects - Finished products, with an old MT date

In 2023 The Danish OMCL initiated a market surveillance study regarding products that have been on the market for many years, and the study was finalized in 2024.

The purpose of this project was to ensure the MAH's followed current requirements. The project involved 4 different products. One of the products was not tested, as MAH submitted new methods and validation reports before the project were started. Laboratory and full documentation control were performed on the remaining 3 products.

For the one of the products, the project was combined with an API control of the API used for the finished product tested. This API control involving testing according to current Pharmacopeia monography for the API, and by our In-House Residual solvent method.

7 different batches of finished products, and 3 API batches were analyzed. The analytical control included ID by UV and IR, Assay by titration, Related substances by HCPL and Residual solvents by GC-MS for the APIs. Assay by HPLC were performed for all finished products, Related substances by HPLC, Friability, Dissolution by UV and disintegration were analyzed for some of them. All results conformed to the specification limits.

The outcome of the project was, for two of the tested products, the validation documentations were not up to date, and MAH was requested to ensure the documentation follows current requirement. Especially, for one of the products, the analysis of Related substances was not performed as the method was by TLC. The MAH have planned to update this method to a more updated method, using HPLC.

Residual solvents

In the fall of 2023 and until the end of 2024 a project where performed to test the content of residual solvents in API using the optimized GC-MS method for the analysis of residual solvents in finished products and API. Samples and MAH were selected based on the risk-based model. In total 14 samples were tested, of 4 products with 8 different MAH and 10 different API production sites. 2 products (3 API sites) where specific to this project, whereas the rest were collected in combination to other national market surveillances studies and MSS ongoing at the same time. All samples complied.

Nitrosamines

In 2024 the Danish OMCL carried out a control of valsartan products on the Danish market. 17 products were screened for nitroso-dimethylamine (NDMA) and nitroso-diethylamine (NDEA) using an in-house method (LC-QTOF MS). None of the products were found to contain either NDMA or NDEA.

Diethylene glycol (DEG) and Ethylene glycol (EG) in Glycerol and finished products.

A project where set up to analyse the impurities diethylene glycol and ethylene glycol on cough medicines on the Danish marked. The project where started based on the medicinal product alert WHO send out in 2022. Of samples to be tested, 6 finished products and 9 API where analysed, whereas 2 of the finished products and 1 API where medicinal products prepared in pharmacies. Both the API Glycerol and finished products were analysed using GC-FID analysis. All results complied with the monograph limits for the API for diehtylen glycol and the ICHQ3 guideline for the ethylene glycol.
More information about the method used is described in section 4.

Biological Laboratory

CAP testing
The Danish OMCL participated in 4 studies in the 2024 CAP program where two studies were finalized in 2024, and 2 studies will be continued in 2025. Three studies were continued from the 2023 CAP program and finalized in 2024.

The Danish OMCL preformed different tests on the samples including potency by different cell assays, capillary Electrophoreses, different HPLC methods (SE-, CEX-, IEC and RP-HPLC), as well as total protein and BET testing. Results were reported to the EDQM.

Collaborative studies
The Danish OMCL participated in the collaborative study for the establishment of filgrastim CRS4 used in the Ph. Eur. Monograph for filgrastim concentrated solution. The final content assignment was calculated from the results from three laboratories.

3.4 General Regulatory Tasks

National Market Surveillance study
Anti-tampering devices (ATD).

In 2023 and 2024 a control project on antitampering devises has been performed by Danish OMCL. The completed project had 213 products from 148 companies called in for a control. Simple or full labelling control and control of the function of the ATD were performed.
Approx. 10% of the packages requisitioned had an ATD that did not work. The flawed devices are designed as a sticker, that can be removed without it being visible on the packaging.
All contacted companies were encouraged to check the ATD on other marketed products than those who were sampled for the OMCL control. Also, an information of the control project was published at the Danish Medicines Agency' webpage.
The general conclusion is that the Danish market is doing well in regard to the quality of anti-tampering devices on marketed pharmaceutical packages.

To highlight the results and share our gained experience the we participated at the CAP-sampler workshop with a presentation together with the Ireland.

Project on Patient information leaflets

A leaflet in Danish has to be uploaded at "Indlaegsseddel.dk" for all products marketed on the Danish marked. In 2024 the Danish OMCL carried out a control project to check:

- Whether the package leaflet is uploaded?
- Whether the package leaflet is printable?
- Whether the package leaflet is readable when printed out?
- Whether the electronic package leaflet contains a date of latest revision?

5% of the leaflets controlled were flawed. 241 searches on "Indlaegsseddel.dk" were made for ATC codes R01 and S01-03, which cover medicinal products for diseases of the nasal cavity and eye and ear diseases. In particular, the font size of several package leaflets was smaller than point 9 as recommended according to the Readability Guideline.

Further ATC groups were selected for continued control projects.

CAP sampling and label check
For centrally authorised products CAP sampling and label check were performed for packages on the Danish marked. Samples were collected from wholesaler level.

In 2024, 4 centrally authorised products were sampled. No non-compliance was detected for these 4 products. For one product the wrong EU number of this product were sampled, however, the sampling and control was continued.

1 generic product were sampled in 2024. Also, with no non-compliance to the label check detected.

5 parallel-distributed products were samples with 2 non-compliances found. For the first one the medicinal formulation was not labelled correct, and the other products did not meet the Danish blue box requirements.

Contribution to the European Pharmacopoeia (Ph. Eur.)
Denmark have 3 delegates in the Ph. Eur. Commission who participate in the tree yearly meetings. Two of these delegates are from the Danish OMCL, and the last is an assessor from the DKMA.

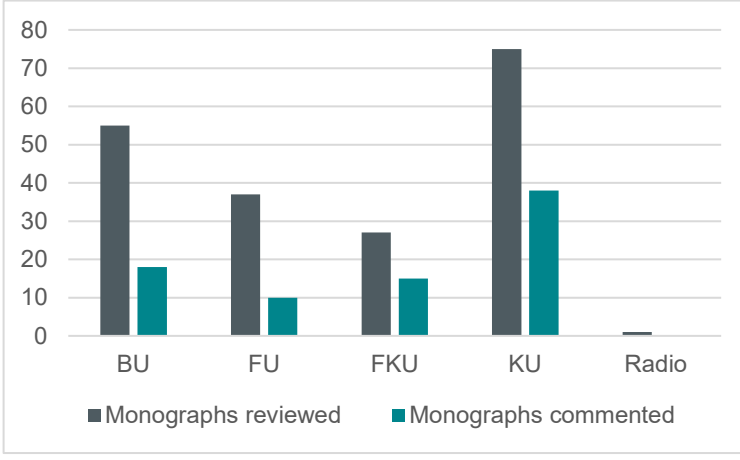
The Danish OMCL also participated in a number of expert groups to Ph. Eur.:

- Gr. 14: Radiopharmaceutical
- CST WP: Chromatographic separation techniques
- CTP WP: Cell Therapy Products
- MAB WP: Monoclonal Antibodies

A substantial part of the Danish activities concerning development of pharmacopoeial monographs (e.g. “Pharmeuropa” evaluation) takes place in the 4 subcommittees for the Danish Pharmacopoeia Commission; Biology Subcommittee (BU), Chemistry Subcommittee (KU), Pharmacy Subcommittee (FU) and Pharmacognosy Subcommittee (FKU). The Danish working group for Radiopharmaceuticals (Radio) have also handled relevant monographs.

The committees consist of participants primarily from industry and academia combined with assessors, regulators and laboratory experts from the Danish Medicines Agency. This composition of participants assures that both purely technical as well as legislative aspects of the monograph proposals are addressed. The committees commented on all four editions of PharmEuropa in hearing during 2024. The number of monographs reviewed and commented is illustrated in Table 3.

TABLE 3
MONOGRAPHS REVIEWED AND COMMENTED BY THE DANISH COMMITTIEES



Source: "Optælling af monografier i høring og kommenteret (2024)"

Explanatory note:
BU: Biology Subcommittee
KU: Chemistry Subcommittee
FU: Pharmacy Subcommittee
FKU: Pharmacognosy Subcommittee
Radio: The Danish working group for Radiopharmaceuticals

The Danish secretariat of the National Pharmacopoeia Authority (NPA) handled 6 Requests for Revision and 2 questions for the content in a monograph in 2024. This has increased compared to 2023 where 4 Requests for Revision and 2 questions were handled, and in 2022 only 1 Request for Revision were handled.

The Danish NPA furthermore handled 9 questions related to The European Pharmacopoeia (Ph. Eur.) or the Danish legislation for quality standards on medicinal compounds and products.

Workshop of OMCL guideline Validation of Computerised Systems

The Danish OMCL has in September 2024 together with EDQM, Croatia, Sweden and the Netherlands contributed to the planning and execution of a 2-day onsite workshop in Strasbourg in the guideline Validation of computerized systems. An online version will be prepared in 2025.

4
Method related activities

In this section, we report some of the highlights from the OMCL's method related activities from 2024.

Diethyleneglycol (DEG) and Ethyleneglycol (EG) in finished products.

The Danish OMCL used the monograph for the API Glycerol as a GC-FID method to test finished products containing glycerol for the content of the impurities DEG and EG. To be able to do this, further validation work on the impurity analysis from the Glycerol monograph has been done according to OMCL and ICH guidelines in according to limit tests. The method where then used in the national control of cough medicines and corresponding API running in 2024 described in section 3.3.

5
Public relation activities

In this section, we report some of the highlights from the OMCL's public related activities from 2024.

The Danish Medicines Agency are working on our communication as one of our four strategic benchmarks "*We will invest in dialogue and communication with the public and society to become the primary source of knowledge on medicines and medical devices*."

In the Danish OMCL we try to communicate about the outcome and learning from finalised control project and our standard practice for different control parameters.

In 2024 we uploaded the following news about control projects at or webpage: News (laegemiddelstyrelsen.dk)

- Completion of the project regarding the control of anti-tampering devices (ATD) on medicinal product packages (laegemiddelstyrelsen.dk)
- Control of companies' upload of package leaflets to the Danish Medicines Agency's portal DKMAnet (laegemiddelstyrelsen.dk)

We republished the following news from EDQM:

- Survey on strategy for Ph. Eur. quality standards for monoclonal antibodies (laegemiddelstyrelsen.dk)

From the Pharmacopoeia Commission session 180 we published the news about the deletion of the pyrogen test in rabbits (only in Danish) "*A milestone for the reduction of the number of laboratory animal*s". This news was also shared at the Danish Medicines Agency' Facebook page and LinkedIn. Furthermore, the news was republished in the Danish media by Pharma-Danmark, Dagens Pharma and Medwatch.

- En milepæl i arbejdet med at reducere brugen af forsøgsdyr i lægemiddelindustrien

The Danish Medicines Agency have multiple corporations and information about our cooperation with Brazil was shared at LinkedIn. The head of the Danish OMCL and our quality person participated in a workshop for 1,5 day in Brazil. The workshop concentrated about risk-based sampling which ANVISA is working on implementing (only in Danish).

- https://www.linkedin.com/posts/laegemiddelstyrelsen_kender-du-hovedstaden-i-brasilien-activity-7174411550860918784-Zlan?utm_source=share&utm_medium=member_desktop&rcm=ACoAACOOAI8BfGlUZ_ntb93KT5VhZUzXOZWDJxU

Furthermore, a virtual workshop with COFEPRIS (Mexico) took place in April 2024. The workshop theme was the control of medicinal products for human use and provided an opportunity to exchange information and experiences.

- One main takeaway from the workshop was that there are many common aspects in laboratory control at both COFEPRIS and the Danish OMCL, e.g. with regard to the quality management system, accreditation system etc.
- COFEPRIS identified the following areas in which further exchange of experiences could add value to their organisation; DKMA's risk assessment, IT-systems, limit values for nitrosamines and laboratory visits.

The biologic team promoted a knowledge toolbox at our webpage for advanced therapy medicinal products (ATMP) which they have composed with a team of experts from all the agency.

- https://www.linkedin.com/posts/laegemiddelstyrelsen_nyt-v%C3%A6rkt%C3%B8j-i-luften-m%C3%A5ske-er-du-activity-7188899497727410176-JH5_?utm_source=share&utm_medium=member_desktop
- Knowledge toolbox for ATMP: Regulation of innovative medicinal products including advanced therapies (ATMP) (laegemiddelstyrelsen.dk)

6
Future planning

In this section some of the future national projects and Network related activities will be enumerated.

On 1 July 2025, Denmark takes over the presidency of the EU. The presidency is represented at the highest level by government members from the country holding the EU presidency. The task is initially to lead the meetings of the Council of Ministers.

The Department of Control and security of supply are going to organise the Working Group of Enforcement Officers (WGEO) meeting of 2025.

6.1 National

The Danish OMCL expect to focus on the following projects on the national marked:

- Follow-up on previous controls to check if the MAH have corrected our findings
- Eye preparations
- Medicinal products that have been approved a very long time ago.
- Heparin project

6.2 Network

The Danish OMCL expect to participate in the following testing:

- MSS065 Alendronic acid tablets, disintegration
- MSSFP006 Lenalidomide
- MSS066 Lenalidomide
- PTS254, PTS255, PTS256, PTS257, PTS258, PTS259, PTS263 and PTS/ILC
- Collaborative study BSP172 Heparin
- CAP sampling and testing

7
Difficulties encountered

The OMCL's difficulties related to testing activities and organisation.

Closure of radiopharmaceutical products analysis in the Danish OMCL

In August 2024, the Danish OMCL received the information that the Danish government had decided to reduce government staff by 1,000 full-time employees in 2025 through a wide range of initiatives across the ministerial areas. As a consequence, at the Danish Medicines Agency, the task of analytical control of radiopharmaceuticals will no longer be performed from 1 January 2025.

As a consequence of this decision, a large period of 2024 have concentrated on the closure of the radiopharmaceutical team. However, the team still made a significant contribution to the control activities, which is described in this report.

The analytical team which performs the control of radiopharmaceuticals has always been considered a "Center of excellence" in Denmark. A Center of Excellence is a team that provides leadership, best practices, support and training for a focus area. This is truly what characterizes the "radiopharmaceutical team" in the Danish OMCL. A well-functioning team of two laboratory technicians and three analytical chemists, who professionally carries out the controls of radiopharmaceuticals in DK and the EU.

The control of the quality of radiopharmaceuticals is often challenging and difficult. The radioactive analyses require very thorough and detailed preparations, and this is carried out in close collaboration between the technicians and the chemists. A summary of the results of the control efforts from the last 3 years shows;

- OOS in 15% of the controls,
- Errors in the documentation in 46% of the controls,
- Errors in 8% of the controls which could affect the stability of the medicine.

The Danish OMCL will continue to be able to carry out other forms of control of the radiopharmaceuticals, just like other medicines. For example, checks of the documentation for method validation, labeling as well as GMP checks with the companies and hospital departments that manufacture radiopharmaceuticals. The Danish OMCL is participating in GMP inspection as ad hoc specialist on the analytical part of the inspection if requested by the inspectors.