

Controlled Drugs in Europe: Regulatory Frameworks, Nasal Administration and Specialist Manufacturing

In clinical settings, morphine and fentanyl have long since established themselves as analgesics of choice.

Meanwhile, cannabis-based products for medicinal use (CBPMs) such as cannabidiol (CBD) and tetrahydrocannabinol (THC) are the subject of increasingly widespread medical attention – not only for pain relief but as treatments for inflammation and to support relaxation and healthy sleep.

However, the illicit opioid epidemic and a burgeoning black market have ramped up regulatory scrutiny on controlled substances such as these. Stringent monitoring govern their manufacture, distribution, and use across Europe, with exacting requirements to ensure safety and security in both EU and non-EU countries.

Nevertheless, the fact remains that many controlled substances are clinically essential. In fact, their strategic importance is expected to grow significantly in coming decades.

The Author

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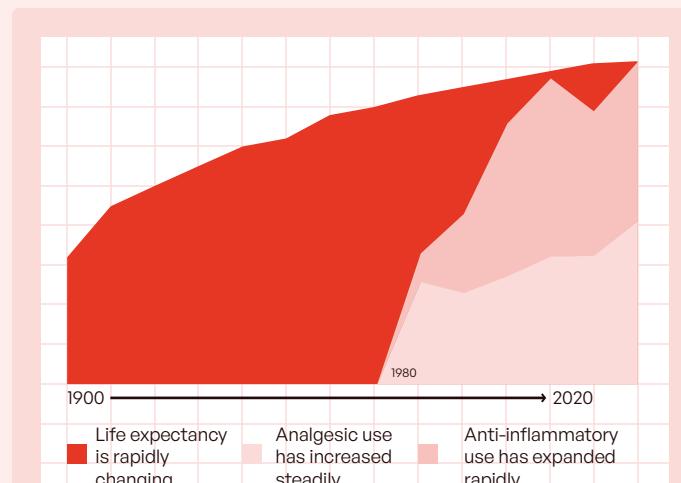


Demand Driven by Demographic Changes

While growing demand for controlled drugs is not limited to Europe, demographic forecasts suggest that demand for these therapies will be particularly pronounced on the European continent.

Like much of the world, Europe is getting greyer: Eurostat projections estimate that the average age in the EU27 will rise from roughly 44 in 2020 to over 48 by 2050. This is driven by Baby Boomers and Generation X reaching old age, with lower birth rates in subsequent cohorts leading to younger generations accounting for smaller proportions of the population.

As the European population grows older, rates of chronic illness are expected to rise – accompanied by a rise in demand for pain management and anti-inflammatory medication. High-potency analgesics also play a vital role in ensuring comfortable and dignified end-of-life and palliative care.



Sources: Our World in Data (life expectancy); OECD Pharmaceutical Consumption Database (DDD per 1,000 inhabitants per day in Europe).

Opioid-based Therapies Offer Proven Clinical Value

The effects of this demographic transition are exacerbated by the rising prevalence of cancers. A recent study led by researchers at

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the Institute of Cancer Research in London identified this rise across all age groups*, with rates still highest in older segments. Given the frequent need for invasive treatment, and the side effects often caused by cancer therapies, the increase in cancer diseases is likely to be accompanied by growing need for pain relief.

In intensive care, too, opioid-based therapies are vital for managing and alleviating severe pain caused by major trauma and surgery. The array of controlled analgesic substances also offers alternative pain relief options for patients unable to tolerate certain compounds due to significant and persistent side effects.

In short, while the public perception of controlled substances may have been shaped and even shaken by media focus on illicit activities, their clinical necessity has been conclusively established over decades. When properly administered in appropriate circumstances, these therapies have the potential to save lives.

*Berrington de Gonzalez et al. (2025) Annals of Internal Medicine. <https://doi.org/10.7326/ANNALS-24-02718>

Growing Acceptance of Nasal Administration

Although widely associated above all with migraine therapies and decongestants, nasal sprays are an increasingly popular delivery method for controlled substances.

The strong blood flow and low enzymatic activity in the nasal passages offer excellent bioavailability, with this rapid absorption key to achieving swift therapeutic effect. What's more, a non-invasive alternative to parenteral administration with comparable efficacy presents obvious advantages in complex and pressurised clinical situations – and neatly eludes the problem of needle-related phobias.



Nasal delivery therefore represents a safe, swift, and well-tolerated administration method. Most importantly, however, regulatory authorities worldwide are increasingly open to the use of nasal administration for high-potency analgesics and CBPMs.

Increasingly Stringent Regulatory Framework

Given their potency and the potential for addiction, controlled substances are subject to strict regulation. Although there is scope for some deviation between countries, especially in the post-Brexit landscape, widespread alignment on controlled drugs exists across Europe.

The EU has embarked on a major reform of existing pharmaceutical legislation, in part in response to illicit opioid manufacturing and supply. The Pharmaceutical Package currently under consideration is the first major overhaul of EU law in this area since 2004 and will undoubtedly have implications for controlled substances. Given the protracted nature of the EU legislative process, the final texts are expected to be adopted in 2026 or 2027.

Controlled substances must be produced and supplied in line with Good Manufacturing Practice (GMP) and Good Distribution Practice (GDP). These frameworks set out minimum quality, safety, and integrity standards throughout the supply chain to ensure proper handling, storage, use, and disposal of controlled drugs.

In the EU and in non-EU countries, companies seeking to manufacture, store, distribute, import, export, or dispense controlled substances must secure specific licences from the relevant national authorities. These licences are usually run for a one-year term and are available from the MHRA in the UK, the HPRA in Ireland, and the Federal Opium Agency (BOPST) in Germany.

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Mandatory inspections are, understandably, a principal element of regulatory monitoring. Besides examining manufacturing and storage facilities, inspectors typically select specific batches of controlled substances and review all pertinent documentation. This includes checking weights throughout manufacturing processes to ensure all materials are duly accounted for, and reviewing proper documentation through the entire chain of distribution, dispensing, and disposal. Significant discrepancies can put companies' licences at risk.

Specialisation Vital to Meet Growing Demands

Regulatory requirements mean that pharmaceutical companies cannot regard controlled drugs as an easy “add-on” to their existing operations. Instead, they require specific consideration and entail considerable investment.

Controlled substances must be manufactured in dedicated facilities, segregated from all other production activities. Enhanced security measures are vital to support traceability and prevent illicit behaviour, such as access control systems in production halls and warehouses. Production waste and unused doses must also be denatured and sent for proper disposal to ensure that no elements can be recovered and exploited for illicit purposes.

Implementing this in practice requires considerable investment, both in physical infrastructure and in skilled personnel.

Qualified specialists must be extensively trained and instructed at every step in the supply chain: production operatives need to control and monitor sophisticated equipment; warehouse and distribution staff must be well versed in safe and secure handling protocols; and pharmacists must dispense and document substances with meticulous precision.

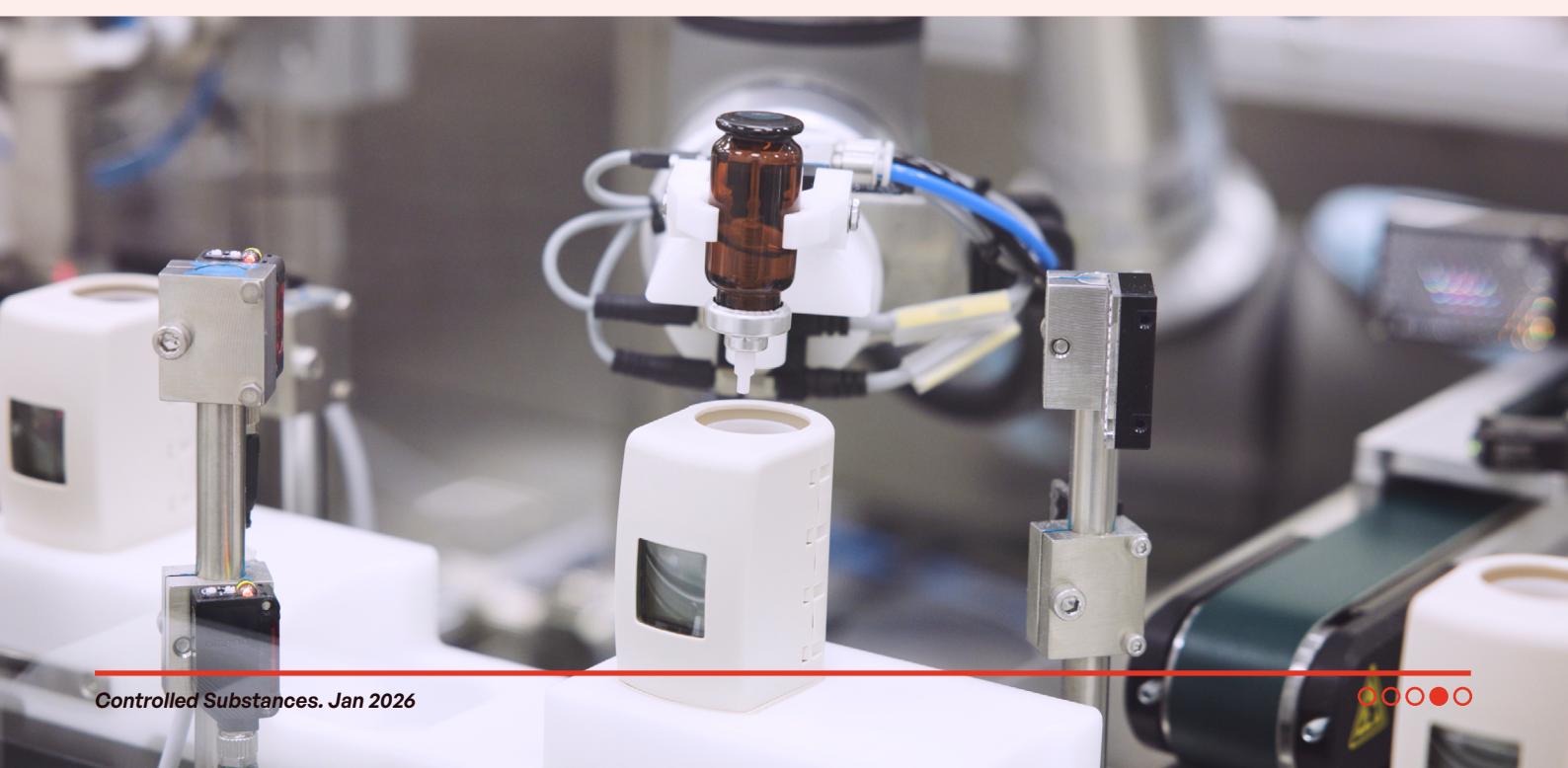
Monitoring and reconciliation are essential at every stage in the supply chain.

Depending on the regulatory regime, companies involved in the manufacture and supply of controlled substances must designate one or more persons to bear responsibility for the overall process. In the UK, for example, Controlled Drug Accountable Officers (CDAOs) are tasked with ensuring legal compliance, complete documentation, and appropriate training throughout a company.

The Challenges of Outsourcing Controlled Drug Manufacturing

Given the cost and complexity of establishing compliant controlled substance manufacturing and securing the requisite approvals, many pharmaceutical and biotech firms seek to outsource these activities. A fundamental problem, however, is a lack of suitably licensed CDMOs in Europe with meaningful production capacity.

While all pharmaceutical manufacturing is subject to strict requirements, CDMOs producing controlled substances must satisfy even higher standards – including in relation to quality assurance, security, transparency, and data integrity. And, given the protracted lead times involved in securing regulatory approvals and licences, and the need to navigate national and EU requirements, this bottleneck is unlikely to ease in the near future.



Curida's Approach to Controlled Drug Nasal Spray Manufacturing

Based in Elverum, Norway, Curida is a CDMO with an impressive track record of manufacturing controlled substances in nasal spray form – and with plans to supplement its portfolio with a range of further therapies

Checklist

10 Key Attributes in a Controlled Substance CDMO Partner

Curida serves as a prime example of a CDMO with the capability to produce numerous controlled substances in nasal-spray form for the European market. Beyond this, Curida is experienced in navigating strict import and export regulations.

Drawing on its example, there are a number of essential criteria that pharmaceutical and biotech firms should look for in a partner for controlled drug manufacturing:

- Regulatory licences for the manufacture, storage, distribution, and import/export of controlled substances
- Segregated manufacturing and storage facilities with effective access controls
- Robust reconciliation systems
- Audited QA, safety, and security management systems
- Extensive experience of controlled drug and nasal spray manufacturing
- Secure waste destruction processes
- Validated workflows, from technology transfer through to series production
- Fully compliant digital documentation and quality management system
- Established European manufacturing footprint

based on controlled substances in the coming years.

Focused primarily on the European market, it has a suite of fully licensed controlled drug facilities, from specialist manufacturing systems through to secure storage. What's more, it has established a strong culture of regulatory compliance and inspection-readiness. Curida's unwavering commitment to compliant handling and reliable safety upholds high quality standards while minimising the risk of disruption.

Put simply, Curida has the experience, expertise, and specialist facilities required to support efficient and controlled drug manufacturing. The Norwegian CDMO covers the entire cycle, from technology transfer through to series production, and can accommodate flexible batch sizes. And, building on its expertise in import and export processes, Curida is ready to support an increasingly international client base.

About Curida[®]

Curida is a trusted CDMO based in Norway, offering end-to-end development and contract manufacturing of both biologics and small molecule sterile and non-sterile liquid pharmaceuticals. With 50 years of expertise in Nasal Spray and Blow-Fill-Seal technologies, Curida supports everything from formulation and tech transfer to commercial scale-up. Its separate Bio-CDMO unit provides manufacturing of monoclonal antibodies for preclinical and diagnostic use.

