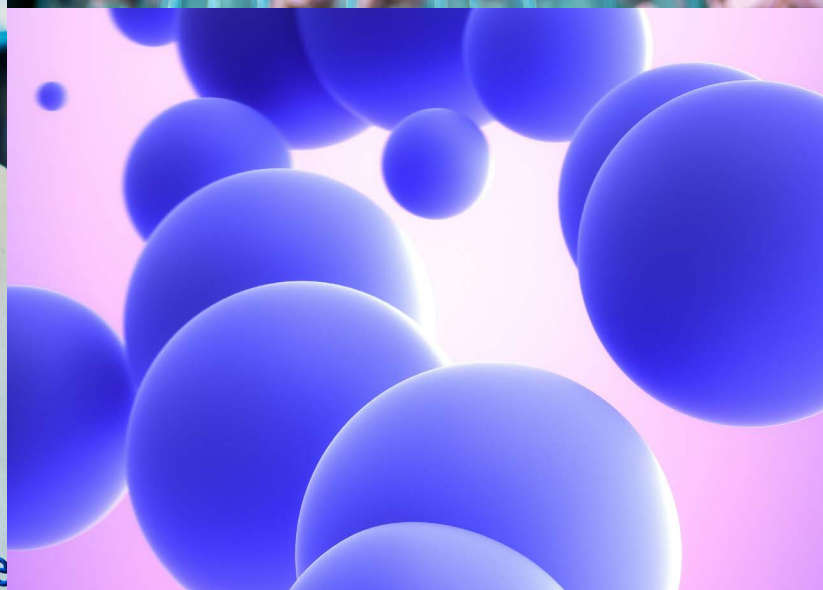
Pfizer CentreOne

Helping deliver a smarter, faster and more patient-centric future for OSD manufacturing



The rapidly evolving oral solid dosage (OSD) landscape

Oral solid dosage (OSD) forms, including tablets, capsules, granules and powders, represent a dominant mode of delivery for medications across a wide range of therapeutic areas, from cardiovascular diseases to various cancers. As a versatile therapeutic modality, OSDs offer a wide range of benefits for both patients and developers, including:

- **Patient convenience:** OSDs are easy for patients to take, transport and store, making them ideal for individuals with busy lifestyles and those requiring self-administration.
- **Precise dosing:** Providing accurate and consistent dosing, OSDs help ensure patients receive the exact amount of medication prescribed.
- **Flexible dosing options:** OSDs can be designed with various release mechanisms (immediate, delayed or extended-release) to suit different therapeutic needs and dosing schedules.
- **Enhanced stability:** OSD formulations generally have longer shelf lives and greater stability compared with liquid medications, reducing the need for refrigeration and ensuring consistent potency over time.
- **Cost-effectiveness:** Compared with other dosage forms, OSD production is typically less expensive.

With these benefits in mind, it is no surprise that OSDs own the title of "the most popular mode of drug delivery worldwide," with demand for this cost-effective and convenient administration option continuing to rise [1]. This is reflected in the global OSD contract manufacturing market, valued at approximately USD 36.50 billion in 2023, and projected to grow at a compound annual growth rate (CAGR) of 5.97% from 2024 to 2030 [2].

Four key trends shaping the future of the OSD space

Meeting the growing demand for OSDs requires more than simply scaling up existing processes. It necessitates a deep understanding of the evolving trends and challenges shaping the OSD landscape and a commitment to innovation. With an appreciation of these trends and their associated challenges, drug manufacturers can proactively adapt their strategies to make production smarter, faster and more patient-centric to ultimately meet the evolving needs of patients worldwide.

Trend 1:

Changing lives by embracing Pharma 5.0 in OSD production

The pharmaceutical industry is under increasing pressure to accelerate drug manufacturing while maintaining the highest standards of quality and efficiency. This demand for speed stems from the urgent need to bring life-saving therapies to patients faster and to respond effectively to emerging health threats.

While Pharma 4.0 represented the integration of digital technologies and data-driven approaches in pharmaceutical manufacturing to enhance efficiency, productivity and quality, the industry is now increasingly looking to adopt a Pharma 5.0 approach [3]. By combining human expertise with digital technologies like artificial intelligence (AI) and machine learning (ML), Pharma 5.0 is set to revolutionize the pharmaceutical industry, enabling a new era of efficiency and patient-centricity in drug manufacturing.

Key elements of Pharma 5.0 that are likely to impact OSD manufacturing include:

- **Robotics and automation:** Robotic systems can automate various tasks in OSD production, such as material handling, blending, compression, coating and packaging. This improves efficiency, reduces human error and increases throughput, ultimately leading to faster production timelines and reduced costs.
- **Real-time monitoring and control:** Integrating sensors and data analytics into OSD production lines enables real-time monitoring of critical process parameters. This allows for immediate identification of deviations and proactive adjustments, helping to ensure consistent product quality and minimize waste.
- **Digital twins:** Creating digital replicas of OSD manufacturing processes facilitates virtual optimization, accelerating timelines while helping to proactively identify and mitigate potential risks.
- **Process analytical technology (PAT):** Advances in PAT and in-line monitoring can enhance product quality by providing real-time insights into critical quality attributes. This enables proactive adjustments to manufacturing processes, helping to ensure consistent product quality and minimizing batch failures.

Transforming OSD manufacturing with Pharma 5.0

Pfizer has spent decades at the forefront of some of the most profound changes in technology and medicine. Staying ahead of the curve, we are embracing Pharma 5.0 by integrating advanced digital technologies and data-driven approaches into our operations.

Leveraging the power of AI and ML, we're optimizing processes to help accelerate development timelines to bring therapies to patients faster and more efficiently.

We utilize AI and ML technologies for automated visual inspection, real-time anomaly detection and rapid root cause analysis, all underpinned by Pfizer's Manufacturing Intelligence Platform. Additionally, our Manufacturing Excellence (IMEx) program combines real-time manufacturing digital systems with our employees' expertise to drive continuous improvement and productivity.

Leveraging PAT to achieve consistent and precise coating

The coating of OSDs serves various purposes, including enhancing the drug product's functionality, stability or patient acceptance. PAT tools, like optical coherence tomography (OCT), are revolutionizing how OSD developers and manufacturers monitor and control coating processes in real time.

In osmotic pump formulations, the coating plays a crucial role in controlling drug release, acting as a semipermeable membrane and allowing water to enter the tablet core but preventing the drug from diffusing out. Applying a very controlled and thin coating layer throughout their manufacture is essential for proper drug release.

OCT technology allows for real-time measurement of the coating thickness on the tablet, enabling immediate adjustments to the coating process if any deviations occur. This ensures that the coating is applied uniformly and meets the required specifications, helping to guarantee consistent product performance and quality.

Leading life science organizations are at the forefront of embracing digital technologies to transform OSD drug manufacturing and enhance their capabilities. AI, ML and digital twin models are rapidly being adopted to optimize processes and accelerate production timelines.

By embracing these advancements, leading organizations are not only enhancing their capabilities but also setting new standards for innovation and efficiency in the pharmaceutical industry.

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Trend 2:

Meeting the growing demand for patient-centricity

Patient-centricity is becoming increasingly important in drug development and OSD formats are well-suited to meet this growing demand, offering ease of administration and the ability for self-administration. There is a growing desire from patients for therapies that seamlessly integrate into their lives, minimizing disruptions and maximizing convenience through:

- Reduced dosage frequency
- Manageable dose size
- Improved taste
- Tailored delivery options designed for specific patient populations

To meet the diverse needs of patients and enhance their treatment experience, developers and manufacturers are producing unique OSD formats leveraging advances in formulation techniques and equipment. These advancements allow for greater flexibility in drug delivery, enabling the creation of tailored solutions that address specific patient needs and preferences. However, each of these formats brings its own production challenges:

Modified-release drugs

Modified-release OSDs, particularly extended-release, offer a significant advantage by reducing dosing frequency and maintaining consistent drug levels in the bloodstream, simplifying medication regimens and improving patient compliance.

However, achieving the desired extended-release profile can be complex, demanding careful selection of polymers, optimization of drug release mechanisms and rigorous testing to ensure consistent drug delivery over time. Osmotic pump formulations, for example, while offering precise control, require specialized equipment like extrusion, spheronization and laser drilling equipment to manufacture.

Mini tablets

These smaller tablets offer an alternative for patients with difficulty swallowing larger OSD forms. Manufacturing mini tablets requires specialized equipment and precise control of size and weight uniformity. Ensuring consistent drug content and release from these smaller units can also be challenging.

Fixed-dose combinations (FDCs)

FDCs combine multiple medications into a single dosage form, simplifying treatment regimens for patients taking multiple drugs. Varied drug dosages and differing material properties within FDCs complicate both formulation and process control, making consistent quality a significant manufacturing hurdle. Achieving uniform drug distribution and managing the complex interactions between the multiple ingredients required necessitates advanced manufacturing techniques and rigorous quality design.

Bilayer tablets

Bilayer tablets offer the unique advantage of delivering two different APIs in a single tablet. This can be used to combine medications with different release profiles or separate incompatible drugs, enhancing both convenience and efficacy. Producing bilayer tablets involves complex manufacturing processes to ensure effective layering and prevent delamination or disintegration.

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Multiparticulates

Multiparticulates, such as pellets or beads, offer flexibility in drug delivery and can be formulated for extended or targeted release. They can also be combined with different APIs in a single capsule to create fixed-dose combinations with improved bioavailability and patient convenience. Multiparticulate development requires specialized techniques, such as extrusion-spheronization, layering or microencapsulation, to ensure consistent size, drug loading, and release characteristics for each pellet or bead.

Coated tablets

Active and solvent coating technologies can mask unpleasant tastes, improve swallowability or achieve modified-release profiles. However, coating processes require careful optimization to achieve the desired thickness, uniformity and functionality. Controlling the release profile of coated tablets, especially for modified-release formulations, demands precise control over coating parameters.

Orodispersible tablets

As these tablets dissolve rapidly in the mouth, they offer a convenient option for patients who have difficulty swallowing traditional tablets or who require a quick onset of action. Producing orodispersible tablets is complex due to the need for specialized equipment and precise control to ensure consistent drug distribution across batches. Water-soluble drugs also pose difficulties during freeze-drying, potentially affecting the tablet's structural integrity, while adherence to FDA size and weight limitations adds further constraints to the manufacturing process.

As OSD products become increasingly personalized, flexibility will be key to ensuring that drug therapies are tailored to individual needs and preferences. This necessitates a deep commitment to innovation and investment in adaptable manufacturing processes.

Help meet patient-centric goals with scale and scope

Powered by Pfizer global expertise, we support OSD needs across a wide range of platforms and technologies, from pellets, tablets and capsules to innovative release profiles.

Tablets

- Immediate-release
- Modified-release
- Bi-layer
- Active-coated
- Sugar-coated
- Dual-active
- Overcoated
- Laser drilling
- Mini
- Enteric-coated
- Sublingual
- Orally disintegrating
- Tablet printing (inkjet and UV)

Capsules

- Immediate-release
- Modified-release
- Pellet-filled
- Powder-filled

Pellets

- Immediate-release
- Modified-release
- Enteric-coated
- Sugar-coated

As an award-winning contract manufacturing organization (CMO), we have an in-depth understanding of the complexity involved in delivering patient-centric OSD formats.

We leverage our extensive experience and specialized capabilities to help identify solutions when manufacturing these formulations to make the complex simple.

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Trend 3:

Overcoming the complex to prevent delays

The production of OSD forms is an intricate journey, marked by various complexities that can potentially lead to delays and hinder the timely delivery of critical therapies to patients. Over the last decade, OSD production has become even more complex, driven by the growing use of challenging active pharmaceutical ingredients (APIs), including those with poor bioavailability and high potency [4,5]. These trends introduce unique hurdles that must be overcome to ensure the safe, effective and efficient production of OSD therapies without delay.

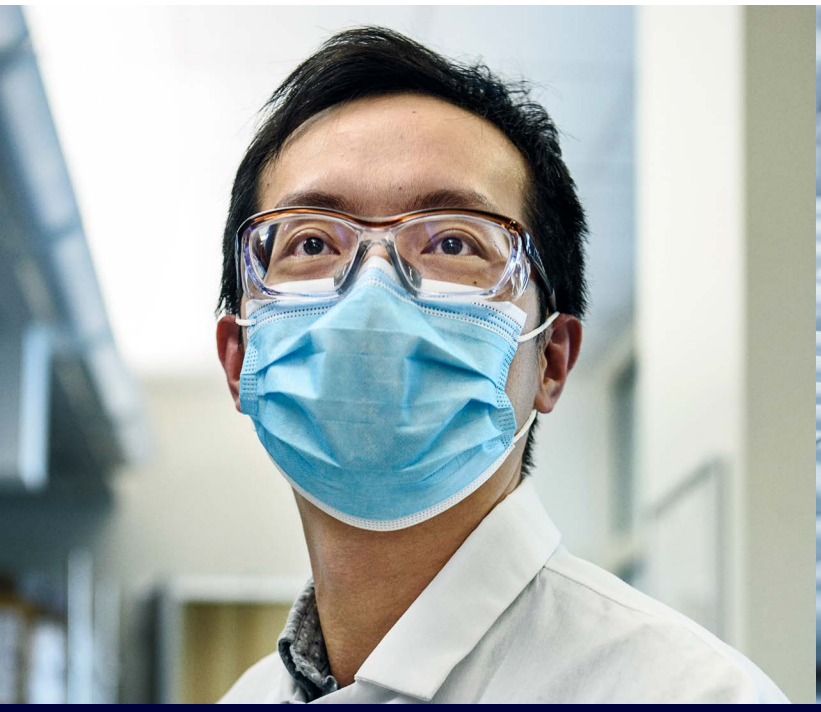
APIs with poor bioavailability

One of the key challenges in OSD production is managing the processing of poorly soluble drugs. These drugs, often classified as Class II or IV in the Biopharmaceutics Classification System (BCS), present manufacturing difficulties due to their inherent properties. This can significantly complicate consistent production and predictable drug release. With approximately 40% of new chemical entities (NCEs) reported as poorly water-soluble compounds, identifying effective manufacturing techniques is more critical than ever [5].

To address the challenge of poorly soluble APIs, drug producers are increasingly turning to innovative processing techniques. Two prominent approaches are particle size reduction, often achieved through milling, and the creation of amorphous solid dispersions, commonly utilizing spray drying technology.

- **Milling:** By physically breaking down API particles into smaller sizes, typically on the micro or nanoscale, milling increases the surface area available for dissolution. This leads to faster dissolution rates and improved solubility.
- **Spray drying:** This technique transforms a liquid feed containing the API into a dry powder by rapidly drying atomized droplets. Spray drying can convert a crystalline API into an amorphous form, significantly enhancing its solubility and dissolution rate. As a valuable tool for bioavailability enhancement, it offers advantages such as continuous operation, scalability and precise control over particle properties.

Selecting the most appropriate strategy to overcome poor solubility requires expertise and an in-depth understanding of the API's physicochemical properties, the desired release profile and the target product profile.



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Highly potent APIs

With estimates suggesting that HPAPIs may now account for more than 30% of the drug development pipeline, the increasing use of HPAPIs in OSD formulations presents unique challenges for and manufacturers [6]. These compounds, often characterized by their significant biological activity at very low doses, present a number of unique challenges throughout production:

- **Operator safety:** HPAPIs can pose significant health risks to operators even at minimal exposure levels. Strict adherence to occupational exposure limits (OELs) and the implementation of appropriate engineering controls are crucial for protecting personnel.
- **Containment:** Preventing the cross- contamination of HPAPIs into other products or the environment is critical for patient safety.
- **Regulatory compliance:** Meeting stringent regulatory requirements set by authorities such as the U.S. Food and Drug Administration (FDA) or European Medicines Agency (EMA) for HPAPI handling and manufacturing can be complex.

By proactively addressing these challenges with a comprehensive approach, drug manufacturers can help ensure the safe and compliant handling of HPAPIs in OSD manufacturing, safeguarding both personnel and product quality.

Expertise to handle the complex

Harnessing Pfizer's global network of specialized OSD facilities designed to minimize the risk of HPAPI exposure and cross-contamination, we prioritize the safe and efficient handling of HPAPIs.

We implement appropriate engineering controls, such as airlocks, room pressure controls, and specialized ventilation systems, ensuring a safe and contained environment for both our operators and your product. With rigorous cleaning and decontamination procedures, we prevent cross-contamination and help to ensure product quality. Our team members also receive extensive training on proper handling procedures, emergency response protocols and the correct use of personal protective equipment (PPE), making them well-equipped to handle your HPAPIs safely and responsibly.

Pfizer's robust quality systems are designed to meet stringent regulatory requirements, including those set by the FDA, EMA and other regulatory bodies. We provide regulatory intelligence for more than 150 countries, helping you navigate the complexity of compliance and regulatory requirements around the globe.

We also hold the necessary licenses and adhere to evolving guidelines on containment, cleaning validation, and operator protection, providing you with confidence in our compliance and commitment to safety.

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Trend 4:

The need to offer greater flexibility in OSD manufacturing and packaging

The future of OSD production hinges on adaptability. Drug manufacturers face the dual challenge of meeting the growing demand for patient-centric formulations while also accommodating increasingly complex compounds. Supporting the increasingly diverse range of OSD formats relies on CMOs with broad expertise and experience across different types of coating, release, milling and drying. They will also need to offer specialized capabilities providing versatility, such as in capsule filling.

The need for flexibility in OSD manufacturing extends beyond drug manufacturing, encompassing the critical aspects of packaging, handling and storage. Each OSD product presents unique requirements, demanding adaptable solutions to help ensure its safe and effective delivery to patients.

Adaptable packaging is crucial in the OSD market, not only to accommodate the diverse needs of different OSD formulations but also to respond swiftly to evolving market demands and regulations. Packaging preferences and regulations can vary significantly across regions and over time, requiring manufacturers to remain flexible and informed to ensure compliance and meet patient needs. For example, different regions may have specific labeling requirements or preferences for packaging formats, necessitating adaptable solutions to ensure successful product distribution and patient access.

Balancing unique packaging needs with reliable supply

To accommodate the diverse needs of OSD products, we offers a wide range of packaging options, including:

- **Versatile formats:** Providing various packaging platforms, such as wallets, bottles and blisters, in different formats and pack sizes to suit different product requirements and market preferences.
- **Customization options:** Offering late-stage customization capabilities, including online printing systems, color differentiation and specialized dose packs, to meet specific branding or regulatory needs.
- **Scalable solutions:** Providing both high-volume and small-volume packaging lines to accommodate varying production scales and market demands.

Flexibility and reliability in packaging

To meet the increasing versatility of OSD forms, we offers a wide range of different packaging lines, from wallets and bottles to blister packs in different formats and sizes.

We deliver the optimum balance between product customization and reliable supply by leveraging late-stage customization, high speed, full track and trace, online printing, hospital unit dose, color differentiation, dose pack and multipack.

To streamline your project's journey to market, we provide services designed to help foster reliability through a "right-first-time" approach. This methodology has led to a strong track record of success delivering on time in full (OTIF) [90-92%], with no issues on audit.

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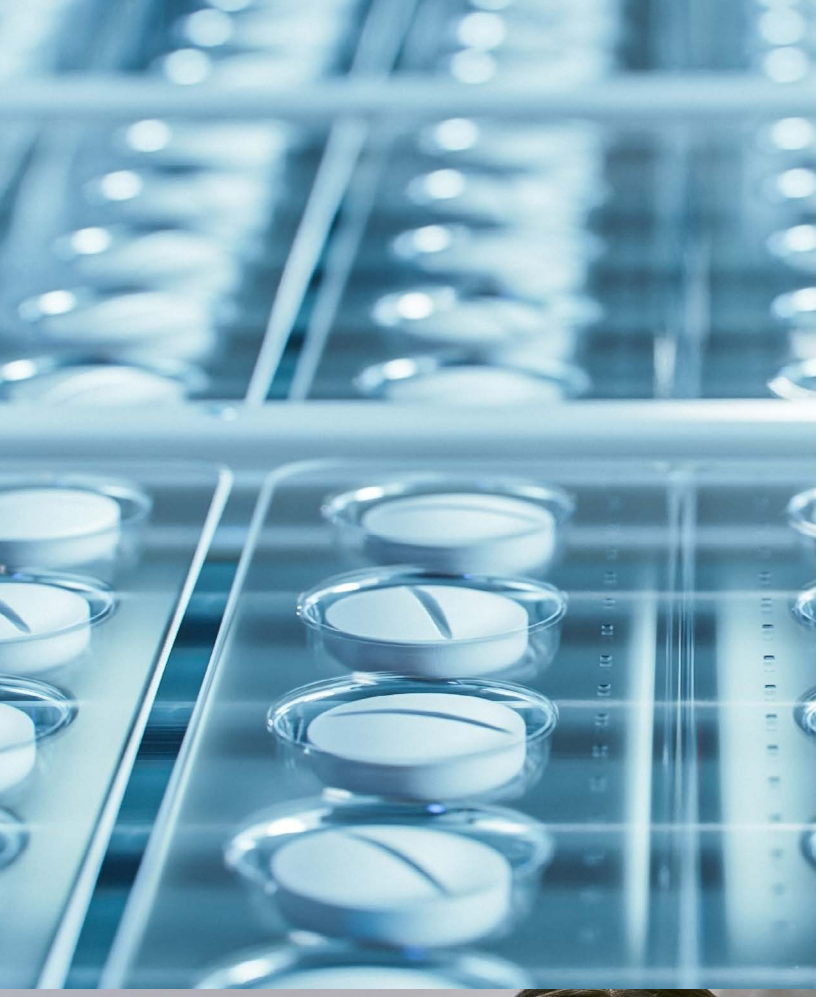

A CMO for OSD therapies that define legacies

The OSD landscape is rapidly evolving, and there is no sign of slowing down. While the potential for patient benefits continues to expand, OSD development and manufacturing complexity are also increasing. To navigate this dynamic landscape and ensure the successful delivery of high-quality OSD therapies to patients, selecting a future-focused CMO partner is essential.

Powered by Pfizer, we are uniquely positioned to meet the evolving demands of the OSD landscape. With a global network of state-of-the-art facilities, coupled with deep expertise in OSD development and manufacturing, we can support a wide range of complex formulations and drug delivery technologies. Leveraging decades of experience successfully delivering high-quality OSD products – including highly potent, cytotoxic, controlled and low-bioavailability drugs, our global Pfizer network of scientific experts can help make the complex simple.

Our team of experts possesses a comprehensive understanding of global regulatory requirements, helping to ensure compliance and facilitate successful market access.

With a strong commitment to innovation, we continuously invest in advanced capabilities and process optimization strategies to help accelerate development timelines, enhance product quality and navigate the future challenges of OSD development and manufacturing.

Find out more about how Pfizer CentreOne can support your OSD journey and make the complex simple.

Discover more →

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For more information, visit
www.pfizercentreone.com/oral-solid-dose

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