

Navigating the Changing Oral Solid Dose Landscape

Oral solid dose (OSD) forms have accounted for the lion's share of the pharmaceutical market for decades, thanks to their easy administration leading to patient convenience benefits, not to mention their shelf-life advantages. As a mature market, it has an unfair reputation for stasis. Much of the innovation spotlight has been on other dosage forms as they have evolved to enhance their own useability, or as they have risen to prominence as a means of enabling the delivery of new therapies, such as biologics.

Despite this, the segment is not standing still. There is considerable innovation going on behind the scenes to provide an ever-improved patient experience and to open the oral delivery route to an ever-expanding array of treatments and molecules, including those not traditionally able to be administered via the GI route.

So, what does the future hold for OSD forms? What challenges face pharmaceutical companies as they try to harness the patient experience benefits of OSD in the future?

Philippe Gorria, Senior Director Formulation Development and Sales, and Dr. Uwe Hanenberg, Head of Product Development at Recipharm, explore the trends shaping the OSD space, discuss the development pitfalls facing the developers of new OSD products, and how to overcome them.

OSD Trends Under the Spotlight

A number of trends are shaping the OSD space at the moment, and look set to transform the segment over the coming years. These include:

- **The Rise of Fixed-dose Combination products to Optimise Patient Centricity** – this has been a trend for several years now, and there is no sign it will be diminishing in importance in the foreseeable future. These formulations allow multiple active pharmaceutical ingredients (APIs) to be combined in a single dosage form, such as a tablet or capsule. They harness modified release

technologies to stagger or delay the release of each API into the bloodstream to minimise side effects or maximise the duration of therapeutic action. As a result, it is possible to reduce the number of doses a patient has to take each day, enhancing convenience and boosting patient adherence.

- **Changing Patient Demands** – by 2030, 1 in 6 people in the world will be aged 60 years or over.¹ As global populations continue to age, patient demands are evolving, requiring OSD drug developers to respond. Older patients present administration challenges, from poor dexterity to issues swallowing. As such, OSD products need to adapt to ensure they continue to meet patient needs – tablets need to be smaller and easier to swallow for example, and packaging needs to be easier for elderly patients to open. Alternatives to tablets and capsules are being explored by drug developers to meet these needs, such as easy-open stick packs containing powdered drug products, designed either to be dissolved in water or swallowed dry. The older cohort isn't the only demographic OSD drug developers need to consider. Younger patients also have unique administration needs to support adherence. For instance, bitter-tasting medicine can be particularly unpleasant for young patients to take – drug developers increasingly need to consider the flavour of their child-centric drug products to optimise patient adherence.
- **Biopharma Continues to Grow** – the global biologics market size is expected to be worth around \$719.84 billion by 2030, expanding growth at a CAGR of 7.8% from 2022 to 2030.² This growth is continuing to impact OSD. Traditionally, biologics had to be administered parenterally, despite the relative inconvenience to patients – the sensitive nature of the active ingredients made them unsuitable for delivery via the gastrointestinal tract. However, advances in OSD technology means that it is possible for some biologics, such as insulin, to be developed for oral delivery, allowing the biopharma space to take advantage

of the patient convenience benefits of OSD. Nevertheless, formulating to enable oral delivery of large molecule products poses challenges that drug developers need to overcome.

- **Small-batch Manufacturing to Support Orphan Drug Production** – The global rare diseases treatment market size was valued at \$119.6 billion in 2021 and is expected to expand at a CAGR of 12.8% from 2022 to 2030.³ This is an exciting area for innovation, but it poses challenges for drug developers – by their nature, these diseases are rare, affecting a small number of people worldwide. As such, new commercial paradigms and manufacturing processes are required to make them financially viable. 3D printing of OSD forms is one option that drug developers are increasingly considering as a means of manufacturing small batches of these, often personalised, medicines as cost-effectively as possible.

The Challenge of Adapting to these Trends

These trends are exciting and offer a wide range of opportunities for OSD drug developers to differentiate themselves from competitors and to deliver drug products that meet the changing needs of patients around the world.

However, developing and manufacturing effective formulations to address these trends does pose challenges for drug developers that need to be overcome.

Formulation Development Challenges

Whether reformulating existing APIs or developing formulations for new molecules, it is crucial that the final OSD formulation meets the specific needs of the active pharmaceutical ingredient to ensure it offers optimum therapeutic performance.

Above all, it is important to understand the physical/powder characteristics of the API, such as particle size, morphology, and solubility. For instance, more and more new Chemical Entities (NCEs) have solubility challenges – if these aren't addressed, along with questions of how to carry drug substance to the right location along the intestinal tract, there can be bioavailability issues



that undermine the ability of the NCE to be delivered orally. The physical characteristics of APIs also drive the selection of excipients and as well as the specific parameters for the final manufacturing process.

Fixed-dose combination formulations can also be challenging. It is important to understand how the different APIs interact with each other, and to understand their therapeutic performance needs to identify potential formulation solutions to achieve optimum effect. One formulation option that is fast gaining popularity as a means of addressing this issue is to use mini-pellets and coated pellets contained within a capsule. These can allow controlled release of multi-APIs to eliminate compatibility issues.

For the new generation of oral biologics, there are two major challenges. The first is ensuring stability of the active in the gastrointestinal tract. The other is absorption into the body, particularly for larger biologic molecules. Actives over 8-12kDa molecular weight cannot be absorbed naturally by the human body, so require active transport systems or tight junction openers to ensure successful oral delivery.

Infrastructure Issues Trying to Adopt New Forms and Packaging Formats

Whether adopting OSD drug products for the first time, or changing to a new OSD form, such as a powder in a stick pack, upgrading manufacturing and packaging lines is crucial. This can take considerable time and financial investment depending on the nature of the line and the needs of the new drug product, as well as its packaging. This can be challenging for pharmaceutical companies to deliver on their own, especially at speed.

Regulatory Difficulties

When formulating a drug product for OSD for the first time, there is a complex range of regulatory challenges that need to be addressed in order to gain approval. Documentation must be able to show that issues such as solubility and bioavailability, as well as API stability have been addressed to ensure optimum therapeutic performance – a particular challenge for OSD forms. Complicating the issue is the lack of harmonisation between different regulatory frameworks – local regulatory knowledge is needed to gain approvals for multiple markets. Drug developers must ensure they

define their regulatory strategy alongside their development approach and deliverables as early in the development journey as possible.

Capacity Issues

Finally, it can be challenging for drug developers to find or build the capacity they need to manufacture high-volume OSD drug products reliably and cost-effectively, particularly if they are doing so for the first time. The new generation of OSD treatments for rare or orphan diseases also face capacity issues, due to their small batch sizes - it can be difficult to find the infrastructure needed to produce at low volumes cost-effectively, undermining the commercial viability of the project.

Overcoming Challenges

These are significant issues that need to be addressed for pharmaceutical companies to develop effective OSD products that offer the convenience and therapeutic performance that patients expect. Harnessing new OSD formulation technologies and presentations can be particularly challenging, particularly for those companies exploring them for the first time.



However, there are expert contract development and manufacturing organisation (CDMO) partners available that can help pharma companies to overcome common OSD development challenges and harness the benefits of the new generation of technologies.

For example, CDMOs with a strong track record in the OSD space can provide dedicated formulation expertise, including insight into the latest techniques, to allow the development of effective orally administered biologics. They can also support in identifying new presentations that may help existing orally administered drug products to stand out in a competitive market. CDMOs with a global footprint can help provide local knowledge about regulations or patient demands to ensure that products meet the requirements of the markets they are intended for.

CDMOs can also support pharma companies in overcoming the infrastructure challenges presented by manufacturing OSD products for the first time, whether at high or low volumes. Those that specialise in the segment will have dedicated manufacturing and packaging infrastructure already in place, which can help pharma companies begin commercial manufacturing with minimal delay.

To meet small-volume project needs, a growing number of CDMOs are investing in small scale manufacturing solutions. E.g., 3D printing is one such option, which can allow the rapid and cost-efficient creation of small numbers of tablets containing precise and consistent doses of API. These tablets can be designed to encapsulate one or more APIs within a complex matrix to control their release, according to the needs of the treatment. Working with partners that offer these advanced technologies, pharma companies can be confident that they have the support they need to deliver small batches or even personalised OSD drug products to treat rare or orphan diseases.

Looking Ahead

As a segment, OSD will continue to grow for the foreseeable future. Their useability and unique patient convenience benefits are compelling, meaning we can expect more and more drug products to be developed with innovative dispersing/delivery devices combined and fine-tuned around the oral route of administration.

Nevertheless, adapting to the changing OSD landscape can be daunting, especially for those drug developers that are harnessing new technologies, or seeking to formulate oral versions of traditionally parenteral drugs. Working with an expert development partner is crucial if pharma companies want to adapt

and thrive in the future pharma climate, and fully harness the unique benefits of OSD.

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Dr. Uwe Hanenberg, Head of Product Development, Oral Solid Dose (OSD) at Recipharm. Uwe is responsible for implementing and executing the OSD Product Development strategy that assures science driven, timely development of new products or services. Uwe has 25 years of experience in the pharmaceutical industry with Bayer, Altana, Grünenthal and Catalent. He has held several leading positions in quality, manufacturing and packaging, product development, project management within the Science & Technology sphere. His areas of expertise are oral formulation development, oral manufacturing technologies, stick pack technologies and pharmaceutical contract services and project management.