Just the Right Dose: The Top Trends Shaping Drug Dosage Forms

As new drug molecules in the pipeline become increasingly complex and approved molecules are reformulated for alternative routes of administration, the drug dosage landscape is shifting significantly. Dr Robert Lee, president, CDMO Division, Lubrizol Life Science Health (LLS Health) discusses the key trends influencing dosage forms in the industry:

1. The 505(b)(2) Pathway

A significant proportion of the innovation in drug dosage form work is being driven by the Food and Drug Administration's (FDA) 505(b)(2) pathway. A 505(b)(2) sponsor can use clinical data produced by other companies to seek FDA approval without performing all the work required with a traditional new drug application (NDA). This is a clear advantage for developers that saves valuable time and money. This strategy also significantly lowers risk since the API being developed has already been used in a marketed product.

As a result, many existing drug products are being reformulated to create new, improved dosage forms, treat different indications, enable new dosing regimens, and achieve new routes of administration via the pathway. This is carried out using advanced formulation technologies to improve existing commercial drugs for new routes of administration or longer-acting dosing regimens that have much better rates of bioavailability and patient compliance.

2. Complex Molecules

As more complex and insoluble molecules have entered the pipeline bioavailability has become a more prevalent formulation challenge. In the past, simply putting a molecule into a tablet may have been effective, but this is no longer the case. Today's molecules require more complex and advanced drug delivery technologies that address insoluble compounds.

It is possible to increase bioavailability through specialist technologies, but to maximise these technologies' effectiveness in a formulation requires expertise and experience. Taking an orthogonal approach and being open to a variety of methods in the early stages of development is also advisable rather than leaning too far towards one approach.

A clear target product profile (TPP) that describes the end drug product is the foundation of good development practice. A profile should include route of administration, dose, form factor, pH, particle size distribution, etc. Once the TPP is understood and the physicochemical characteristics of the active are identified, suitable drug delivery technologies that may achieve the TPP can be deployed. When these technologies are ineffective, creating proprietary technologies to help achieve the objectives can also be explored.

3. More Convenience

Development of combined, implantable polymeric dosage forms has been a growth area since it was first demonstrated that the release rates and therapeutic delivery of drugs could be controlled with highly refined polymers. One of their great advantages is they can be designed to achieve various sustained drug release rates and profiles in line with the requirements of a given patient population.

Drug-eluting devices (DEDs) also provide other advantages over conventional dosage forms: a localised, more targeted delivery, lower dosage requirements, and most importantly, greater patient compliance and convenience.

Implantable DEDs are considered combination products comprising "two

or more regulated components, i.e., drug/device, biologic/device, drug/biologic, or drug/device/biologic, that are physically, chemically, or otherwise combined or mixed and produced as a single entity."

DED developers today have a range of materials and modelling techniques available that improve the efficiency and success rate of creating these products. Through careful selection of excipients, device design, and processing methods, DED developers can optimise delivery of their specific drug. As polymer selection and device design continue to improve with customised chemistries and advanced modelling, DEDs will continue to grow in use.

4. Patient-centricity

It is critically important to take a patient-centric approach to drug delivery. If a patient does not like the dosage form then they are unlikely to take the drug, leading to negative therapeutic outcomes. Dosage forms should appeal to, not repel, the target audience. So, for paediatric medicines, for example, this means creating palatable, oral liquid forms that negate the need for large tablets.

Similarly, parenteral dosage forms are often unpopular and in certain cases may be possible to avoid. The nasal route of administration is a growing alternative for therapies targeting the central nervous systems, thanks to its ability to bypass the blood-brain barrier. It offers great potential for drugs that treat conditions like migraines, allergies, and epilepsy.

The 505(b)(2) pathway is leading drug innovators to rethink existing market medicines and reformulate them in ways that place a greater emphasis on patient-centricity. This is leading to innovations such as long-acting injectables that require a lower dosing regimen or improving the bioavailability of a drug so it can be delivered via an alternative, more convenient route of administration.

5. Regulation

More complex dosage forms, such as long-acting injectables or DEDs, require a very thorough understanding of the manufacturing processes involved to carry out the necessary regulatory characterisation and analytical work. Standard methods to measure the dissolution and elution profile of complex products, for example, will not always work and specialised expertise is required to ensure that such work is completed correctly.

Working with an outsourcing partner for the formulation and development of drug dosage forms can give pharmaceutical companies access to the expertise and technologies to select the best dosage form for each application. CDMO expertise is particularly critical for non-conventional dosage forms, such as nasal and ophthalmic, and implantable devices and depots, which have additional complexity and regulatory issues for drug developers to consider.

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Dr. Lee is responsible for product development. Before joining LLS Health, Rob held senior management positions at Novavax, Inc., Lyotropic Therapeutics, Inc., and Imcor Pharmaceutical Co. He holds BSs in Biology and Chemistry from the University of Washington and a PhD in Physical Bioorganic Chemistry from the University of California, Santa Barbara. Rob has published articles in numerous peer-reviewed journals and three book chapters plus holds 11 issued patents and 14 provisional or PCT patent applications. He has over 23 years of experience in pharmaceutical research and development of both therapeutic drugs and diagnostic imaging agents. Rob maintains strong academic ties, including an appointment as Adjunct Associate Professor of Pharmaceutical Chemistry at the University of Kansas in 1992, and serving as a reviewer for both the International Journal of Pharmaceutics and Journal of Pharmaceutical Sciences.