

A Q&A

Trends and Challenges in Outsourced Oral Solid Dosage Forms



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Combination drugs, ingestible sensors, and targeted delivery are the future of pharma.

As drug companies have fewer and fewer new compounds entering their R&D pipelines, outsourcing of development and manufacturing activities for oral solid dosage forms and sterile forms is on the rise. *Pharmaceutical Technology* recently spoke with Anil Kane, PhD, MBA, executive director and global head of technical and scientific affairs at Patheon, about trends and significant changes in outsourcing the manufacture and development of solid oral dosage forms.

Pharmaceutical Technology: What have been the most significant changes in outsourced oral solid dosage forms over the past decade? What are the current trends?

Kane: The shrinking new drug discovery pipeline has led to significant changes in dosage form development and manufacturing strategies. Existing molecules are being evaluated for newer indications in the same or different therapeutic categories. Fixed-dose combinations of new drug entities combined with off-patent drug candidates for synergistic effects or other clinical benefits are also under evaluation. And, pediatric-friendly formats such as sprinkles, mini-tablets, and orally disintegrating tablets are gaining popularity.

In addition, the demand for life cycle management strategies such as pediatrics, controlled-release dosage forms, fixed-dose combinations, and formats such multi-layer tablets or multiparticulate capsules is increasing.

Due to more stringent regulatory requirements, developers need to apply a much higher level of product and process understanding and robustness justification by using systematic scientific- and risk-based approaches as well as the principles of quality by design (QbD).

Additionally, increased use of highly potent compounds has led to the need for full containment, process automation, closed-loop product transfers between processes, barrier isolators, and equipment with clean-in-place and wash-in-place capabilities. Moreover, early-stage investment in and adoption of continuous manufacturing is gaining popularity. Finally, there is a need to address data integrity requirements, resulting in more automation, data capture, documentation control, and training to imbibe the culture of quality.

Pharmaceutical Technology: Can you highlight any changes you have seen in life cycle management strategies?

Kane: Some of the most widely used life cycle management strategies are pediatric, controlled-release dosage forms, and fixed-dose combinations. Pediatric formulations, particularly in

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terms of palatable powder for reconstitution, sprinkles, dis-solvable tablets or mini-tablets, and chewable soft gels, are becoming increasingly popular.

Controlled-release technologies are a frequently applied life cycle management extension strategy. These technologies have apparent benefits in delivering drugs over an extended period of time, reducing the frequency of dosing and improving patient compliance. Another life cycle management strategy is solubility enhancement, thereby potentially lowering the dose of existing drugs.

Pharmaceutical Technology: What trends has Patheon seen in controlled-release dosage form development?

Kane: In the last three to five years, we have experienced an increase in the demand for dosage forms that exhibit an enteric release followed by an immediate-release portion and then a slow release of the drug over a specified period of time. These delivery systems could be for the treatment of irritable bowel syndrome, ulcerative colitis, Crohn's disease, or certain types of cancers in the lower part of the GI tract.

The benefits of these oral drug delivery systems are that drugs can act locally as well as systemically by getting partially or completely absorbed at the site of action, thus improving therapeutic effect. Dosage forms that have been formulated to deliver such drug candidates include enteric-coated controlled-release tablets, or pulsatile-release beads in the form of extruded beads, pellets, and capsules.

Pharmaceutical Technology: What is the effect of mergers, acquisitions, and licensing deals on an outsource partner?

Kane: The mergers and acquisitions as well as in- and out-licensing activity in the pharmaceutical industry continue to grow. As more clinical candidates are outsourced, Patheon has seen that clinical candidates and the drug products are licensed out by small or emerging companies to large

companies or biotech companies, and then get acquired by other pharma companies. But, the programs stay with us despite change of ownership. In the past three to five years, we have seen more than 55 programs licensed out between Phase I to Phase III, but these programs have continued at Patheon and we continue supporting these programs from clinical through registration and then commercial launch, and resupply. This ensures continuity of supply, as well as avoids loss of know-how and product knowledge.

Pharmaceutical Technology: What are future trends you expect in the pharma industry?

Kane: I believe there will be more emphasis on continuous manufacturing of solid oral dosage forms. The industry will slowly embrace the long-term benefits of continuous manufacturing and will invest in this model to develop clinical and commercial products.

- There will be emphasis on patient-friendly dosage forms, reducing pill burden, addressing the problem of polypharmacy, and improving patient compliance.
- Combinations of drugs and devices will bring several benefits to patients.
- Drugs targeted to specific sites of activity or absorption will enhance the therapeutic effect use of biodegradable sensors, imaging techniques, and application of medical and pharmaceutical electronics to deliver drugs accurately and at a pre-determined rate for enhanced efficacy.
- Ingestible sensors could monitor the compliance of drug administration and drug misuse.
- Technological advances can help personalized therapy and delivery of the right drugs for improving therapy.

Patheon is a leading global provider of pharmaceutical development and manufacturing services. With approximately 8,700 employees worldwide, Patheon provides a comprehensive, integrated and highly customizable set of solutions to help clients of all sizes satisfy complex development and manufacturing needs at any stage of the pharmaceutical development cycle.