Exploring New Potential Through 505(b)(2)

When filing for a drug product approval via the 505(b)(2) regulatory pathway rather than a traditional development pathway, companies are afforded several advantages. The pathway — which was established, along with the 505(j), by the 1984 Hatch-Waxman Amendments of the Federal FD&C Act (the addition of the Drug Price Competition and Patent Term Restoration sections) — offers companies a streamlined route for drug approval.

The 505(b)(2) pathway is a New Drug Application (NDA); however, unlike the traditional route of regulatory approval through the 505(b)(1), companies can submit existing safety and efficacy data of listed drugs in their reports to accelerate their submission and approval process.

Below is an overview of the three statutes that govern the approval pathways:

1. The regular route for novel drug entities that have not received prior regulatory approval or have not been studied previously is the 505(b)(1). This high-risk, high-reward investment is both time intensive and costly to complete and requires the establishment of full safety and efficacy data of the molecule for a specific disease. Drug development of novel drug entities, following this pathway,

can take 10–15 years in total to complete and not much assurance that the regulatory approval will be achieved in the end.

2. An accelerated route to launch can be provided by the 505(b)(2), which leverages existing data from safety and efficacy studies. Following this pathway, and dependent on a few factors, companies can reduce the development timeframe to 2–4 years. It is key for drug sponsors to demonstrate a significant modification — such as change of dosage, formulation, route of administration, new indications, changing from prescription to OTC, new combinations (including two separately approved active pharmaceutical ingredients (APIs), or substitution of an API in a combination product — to the existing drug.

3. The 505(j) route is form of Abbreviated New Drug Application (ANDA) whereby companies will seek approval for a generic version of an already approved innovator drug product. While there can be slight differences in size or shape, the generic must have the same active ingredient as the innovator product and should demonstrate bioequivalence.

If the 505(b)(2) NDA is approved, the developer may be guaranteed between 3–7 years of market exclusivity — five years for a drug that hasn't been approved before in any form, three years for drugs that have been approved before, and seven years for orphan drugs. For smaller or mid-sized companies that have limited R&D capital and resources, it can be advantageous to use the 505(b)(2) pathway for their new drug development or to simply repurpose or reposition a marketed drug. Patent extensions to other indications are commonly used to extend regulatory exclusivity. The FDA approves more NDAs via the 505(b)(2) pathway compared with the 505(b)(1) each year.

Repurposing or Repositioning a Drug

Repurposing or repositioning an existing drug product involves the exploration or expansion of its potential — improving efficacy, formulation, safety, or expanding indications. For sponsor companies pursuing the 505(b)(2) pathway to repurpose or reposition a drug, the process is simplified if the drug has already been approved by the FDA and the route of administration and dosage of the innovator product are maintained.

However, for drug products that have insufficient published literature to support safety and efficacy, as required by the FDA for approval, the sponsor company would need to conduct pre-clinical and clinical research.

The FDA provides detailed guidance on applications and process details for the 505(b)(2) pathway.

Coated Multiparticulates: A Flexible Technology, Ideal for Product Enhancement

Coated multiparticulate (MP) drug delivery systems offer a versatile platform for enhancing the pharmacokinetic, safety, and usability profiles of existing pharmaceutical products. In the context of 505(b)(2)

new drug applications, these technologies enable strategic formulation modifications that may yield clinically meaningful improvements while leveraging previously established safety and efficacy data. By modulating the release characteristics of the API, coated MPs allow for precise control over drug absorption kinetics, providing opportunities to improve safety through attenuation of peak plasma concentrations (C_{max}) mitigation of food effects, and reduction in drug-drug interactions.

Safety-related enhancements are particularly salient in cases where the reference listed drug (RLD) exhibits undesirable pharmacokinetic variability or a narrow therapeutic window. By employing sustained-release or enteric coatings, MPs can dela rse events and improving the therapeutic index. Furthermore, by decoupling drug absorption from the fed or fasted state, MPs may significantly diminish the impact of dietary factors on bioavailability. Similarly, temporal separation of absorption windows can minimize interactions with metabolic enzymes and transporters in the gastrointestinal tract, reducing the potential for clinically significant drug-drug interactions.

In parallel, MP-based dosage forms can improve patient compliance by enhancing the convenience and flexibility of administration. Multiparticulate formulations can be incorporated into sprinkle capsules, oral powders, or sachets, facilitating use in pediatric, geriatric, and dysphagic populations. The modular nature of MPs also allows for the development of extended-release profiles that support once-daily dosing regimens, thereby enhancing adherence. Notably, formulations that obviate the need for food-related dosing restrictions further simplify patient instructions and reduce the risk of administration errors.

From a commercial and regulatory perspective, coated MPs enable value-added product differentiation and support effective lifecycle management strategies. By enabling the design of novel dosage forms or fixed-dose combinations of otherwise incompatible APIs, MP systems expand the therapeutic reach of existing drugs. These innovations are particularly well aligned with the 505(b)(2) regulatory pathway, which permits streamlined development programs when sufficient bridging data can be generated to demonstrate bioequivalence or therapeutic equivalence to the RLD. Moreover, MP-enhanced formulations that address previously unmet needs may qualify for regulatory exclusivity and support new intellectual property claims, reinforcing competitive positioning in the marketplace.

In summary, coated multiparticulate technology represents a scientifically and commercially attractive strategy for improving the clinical utility of existing therapeutics. When applied judiciously within a 505(b)(2) framework, these systems can enable differentiated products with enhanced safety, tolerability, and patient-centricity—while optimizing regulatory efficiency and market opportunity.

Bend Bioscience has over 30 years of experience and has worked on dozens of products that utilize the coated MP platform. With this experience and infrastructure, plus a wholly US-based operation, Bend Bioscience is the ideal partner for customers that are interested

in evaluating new formulation options for the 505(b)(2) filing pathway. Our science-based approach to the formulation design and scale-up, combined with the decades of commercial production with impeccable regulatory history continue to lead to seamless product launches and uninterrupted supply.

Bend Bioscience

Formed from three specialist CDMOs, the new Bend Bioscience offers bigger solutions and bolder science across small molecule capabilities and enabling technologies. From pre-clinical to commercial scale, Bend provides its clients with the highest levels of service and science, combining the broad capabilities of a large CDMO with the flexibility and speed of an expert partner. With extensive experience and expertise in developing and manufacturing products utilizing 505(b)(2) regulatory pathway, we can assist you at every step from the development of the formulation and analytical method, cGMP manufacturing of the product for bioequivalence or registration, preparing and submitting IND application to NDA consultation, planning and preparation of the regulatory document, support for responding to the FDA's questions during the review process and post-approval product management. Bend has a team of regulatory experts ready to partner with you through your drug approval process.

For more information or to discuss how Bend Bioscience can help Make Your Medicines Remarkable, contact us:

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