

Project Case Summary

CMC and Global Regulatory Support for Generic Tablet

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Client:	<i>Small U.S. company specializing in acquiring, developing, and marketing select generic products for approval in the U.S., EU, and other countries</i>
FDA Reviewing Division:	<i>Office of Generic Drugs</i>
Project Profile:	<i>Immediate release tablet (three strengths)</i>

1. Planned drug development and regulatory strategy with client
2. Maintained complete regulatory file
3. Prepared, reviewed, and submitted regulatory documentation to FDA on client's behalf
4. Chemistry, Manufacturing, and Controls
 - a. Drug Substance
 1. Advised client of activities performed by drug substance contract manufacturer through commercial scale-up batches and process validation
 2. Prepared and submitted U.S. DMF on behalf of the client
 3. Prepared and coordinated responses to FDA regarding DMF questions. Interacted with three separate companies to coordinate responses to FDA.
 4. Reviewed and commented on EU DMF for contract manufacturer
 5. Performed CGMP audits and Pre-Approval Readiness Program of drug substance manufacturer
 6. Participated in successful Pre-Approval Inspection of drug substance manufacturer (no Form FDA 483 observations)
 7. Reviewed annual reports and amendments to U.S. DMF
 - b. Drug Product
 1. Advised client of activities performed by drug product contract manufacturer: formulation development, pilot scale, and clinical supply manufacture for bioequivalence studies, through commercial scale-up batches and process validation
 2. Advised in batch record creation and review, analytical method validation, manufacturing process protocol development and review, and review of process validation reports
 3. Prepared CMC section of ANDA and MAA applications
 4. Performed CGMP audit of drug product manufacturer
5. Abbreviated New Drug Application
 - a. Prepared complete electronic ANDA (e-ANDA format) for client review and submission to FDA
 - b. Managed overall completion of ANDA (multiple parties were involved in review of various sections of ANDA)
 - c. Prepared draft labeling of the drug product, which included package insert, medication guide, and container labels based on the approved reference-listed drug

- d. Prepared labeling sections of the ANDA in addition to the side-by-side comparison to the reference-listed drug
 - e. Reviewed bioequivalence study report and prepared bioequivalence summary for ANDA
 - f. QA reviewed complete ANDA, including clinical study reports
 - g. Electronically published and submitted ANDA on client's behalf
 - h. Prepared and submitted seven ANDA Amendments during the review process in response to FDA questions regarding labeling and bioequivalence. There were no questions related to CMC.
6. ANDA Post-Approval Support
- a. Product was approved by FDA in 11 months. Provided responses to FDA regarding labeling and bioequivalence questions.
 - b. Prepared and submitted three Supplements (one for labeling changes, one for submitting Structure Product Labeling [SPL], and one for optional bulk packaging)
 - c. Reviewed change control requests from manufacturing and packaging site to determine regulatory impact and approved them
 - d. Prepared Prior Approval Supplement for drug product manufacturing site change (in progress)
7. Marketing Authorization Application
- a. Prepared CMC Section of MAA for client review (currently under review by Dutch regulatory authorities)
 - b. Advised client of changes required of conversion from ANDA to MAA in order to meet EU requirements and developed strategies to meet these requirements

Outcome:	<i>ANDA was approved by FDA in 11 months. MAA submitted and under review.</i>
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