

<ul style="list-style-type: none"> • Most-recent division-proposed labeling (only if generated after latest applicant submission of labeling) 	
<ul style="list-style-type: none"> • Most recent submitted by applicant labeling (only if subsequent division labeling does not show applicant version) 	
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	
<ul style="list-style-type: none"> • Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable 	
<ul style="list-style-type: none"> ❖ Labels (full color carton and immediate-container labels) (write submission/communication date at upper right of first page of each submission) 	
<ul style="list-style-type: none"> • Most-recent division proposal for (only if generated after latest applicant submission) 	4/27/09
<ul style="list-style-type: none"> • Most recent applicant-proposed labeling 	4/26/09
<ul style="list-style-type: none"> ❖ Labeling reviews (indicate dates of reviews and meetings) 	<input type="checkbox"/> RPM <input type="checkbox"/> DMEDP <input type="checkbox"/> DRISK <input checked="" type="checkbox"/> DDMAC 4/17/09 <input type="checkbox"/> CSS <input checked="" type="checkbox"/> Other reviews DMEPA, 4/1/09
<ul style="list-style-type: none"> ❖ Proprietary Name <ul style="list-style-type: none"> • Review(s) (indicate date(s)) • Acceptability/non-acceptability letter(s) (indicate date(s)) 	3/16/09, 1/10/06 4/9/09
Administrative / Regulatory Documents	
Administrative Reviews (e.g., RPM Filing Review ⁴ /Memo of Filing Meeting) (indicate date of each review)	4/24/06
<ul style="list-style-type: none"> ❖ NDAs only: Exclusivity Summary (signed by Division Director) 	X Included
<ul style="list-style-type: none"> ❖ Application Integrity Policy (AIP) Status and Related Documents www.fda.gov/ora/compliance_ref/aip_page.html 	
<ul style="list-style-type: none"> • Applicant in on the AIP 	<input type="checkbox"/> Yes X No
<ul style="list-style-type: none"> • This application is on the AIP <ul style="list-style-type: none"> ○ If yes, Center Director's Exception for Review memo (indicate date) ○ If yes, OC clearance for approval (indicate date of clearance communication) 	<input type="checkbox"/> Yes X No <input type="checkbox"/> Not an AP action
<ul style="list-style-type: none"> ❖ Pediatric Page (approvals only, must be reviewed by PERC before finalized) 	X Included
<ul style="list-style-type: none"> ❖ Debarment certification (original applications only): verified that qualifying language was not used in certification and that certifications from foreign applicants are cosigned by U.S. agent (include certification) 	X Verified, statement is acceptable
<ul style="list-style-type: none"> ❖ Postmarketing Requirement (PMR) Studies 	X None
<ul style="list-style-type: none"> • Outgoing communications (if located elsewhere in package, state where located) • Incoming submissions/communications 	
<ul style="list-style-type: none"> ❖ Postmarketing Commitment (PMC) Studies 	X None
<ul style="list-style-type: none"> • Outgoing Agency request for postmarketing commitments (if located elsewhere in package, state where located) 	

⁴ Filing reviews for other disciplines should be filed behind the discipline tab.

<ul style="list-style-type: none"> Incoming submission documenting commitment 	
Outgoing communications (<i>letters (except previous action letters), emails, faxes, telecons</i>)	X
❖ Internal memoranda, telecons, etc.	X
❖ Minutes of Meetings	
<ul style="list-style-type: none"> PeRC (<i>indicate date; approvals only</i>) 	<input type="checkbox"/> Not applicable 3/25/09
<ul style="list-style-type: none"> Pre-Approval Safety Conference (<i>indicate date; approvals only</i>) 	X Not applicable.
<ul style="list-style-type: none"> Regulatory Briefing (<i>indicate date</i>) 	X No mtg
<ul style="list-style-type: none"> Pre-NDA/BLA meeting (<i>indicate date</i>) 	4/20/05
<ul style="list-style-type: none"> EOP2 meeting (<i>indicate date</i>) 	X No mtg
<ul style="list-style-type: none"> Other (e.g., EOP2a, CMC pilot programs) 	NA
❖ Advisory Committee Meeting(s)	X No AC meeting
<ul style="list-style-type: none"> Date(s) of Meeting(s) 	
<ul style="list-style-type: none"> 48-hour alert or minutes, if available 	
Decisional and Summary Memos	
❖ Office Director Decisional Memo (<i>indicate date for each review</i>)	X None
Division Director Summary Review (<i>indicate date for each review</i>)	5/1/09
Cross-Discipline Team Leader Review (<i>indicate date for each review</i>)	4/30/09, 4/7/06
Clinical Information⁵	
❖ Clinical Reviews	
<ul style="list-style-type: none"> Clinical Team Leader Review(s) (<i>indicate date for each review</i>) 	
<ul style="list-style-type: none"> Clinical review(s) (<i>indicate date for each review</i>) 	4/7/06
<ul style="list-style-type: none"> Social scientist review(s) (if OTC drug) (<i>indicate date for each review</i>) 	X None
❖ Safety update review(s) (<i>indicate location/date if incorporated into another review</i>)	Clinical review
❖ Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, review/memo explaining why not	Clinical review
❖ Clinical reviews from other clinical areas/divisions/Centers (<i>indicate date of each review</i>)	X None
❖ Controlled Substance Staff review(s) and Scheduling Recommendation (<i>indicate date of each review</i>)	X Not needed
❖ Risk Management <ul style="list-style-type: none"> Review(s) and recommendations (including those by OSE and CSS) (<i>indicate date of each review and indicate location/date if incorporated into another review</i>) REMS Memo (<i>indicate date</i>) REMS Document and Supporting Statement (<i>indicate date(s) of submission(s)</i>) 	X None
❖ DSI Clinical Inspection Review Summary(ies) (<i>include copies of DSI letters to investigators</i>)	2/1/06
Clinical Microbiology <input type="checkbox"/> None	
❖ Clinical Microbiology Team Leader Review(s) (<i>indicate date for each review</i>)	X None

⁵ Filing reviews should be filed with the discipline reviews.

Clinical Microbiology Review(s) (indicate date for each review)	4/29/09, 4/5/06
Biostatistics <input type="checkbox"/> None	
❖ Statistical Division Director Review(s) (indicate date for each review)	X None
Statistical Team Leader Review(s) (indicate date for each review)	X None
Statistical Review(s) (indicate date for each review)	4/6/06
Clinical Pharmacology <input type="checkbox"/> None	
❖ Clinical Pharmacology Division Director Review(s) (indicate date for each review)	X None
Clinical Pharmacology Team Leader Review(s) (indicate date for each review)	X None
Clinical Pharmacology review(s) (indicate date for each review)	4/6/06
❖ DSI Clinical Pharmacology Inspection Review Summary (include copies of DSI letters)	X None
Nonclinical <input type="checkbox"/> None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) (indicate date for each review)	X None
• Supervisory Review(s) (indicate date for each review)	X None
• Pharm/tox review(s), including referenced IND reviews (indicate date for each review)	2/10/06
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer (indicate date for each review)	X None
Statistical review(s) of carcinogenicity studies (indicate date for each review)	X No carc
❖ ECAC/CAC report/memo of meeting	X None Included in P/T review, page
❖ DSI Nonclinical Inspection Review Summary (include copies of DSI letters)	X None requested
CMC/Quality <input type="checkbox"/> None	
❖ CMC/Quality Discipline Reviews	
• ONDQA/OBP Division Director Review(s) (indicate date for each review)	X None
• Branch Chief/Team Leader Review(s) (indicate date for each review)	X None
• CMC/product quality review(s) (indicate date for each review)	3/26/09, 4/6/06
• BLAs only: Facility information review(s) (indicate dates)	NA
❖ Microbiology Reviews	
• NDAs: Microbiology reviews (sterility & pyrogenicity) (indicate date of each review)	4/15/09
• BLAs: Sterility assurance, product quality microbiology (indicate date of each review)	NA
❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer (indicate date of each review)	X None
❖ Environmental Assessment (check one) (original and supplemental applications)	
X Categorical Exclusion (indicate review date)(all original applications and all efficacy supplements that could increase the patient population)	
<input type="checkbox"/> Review & FONSI (indicate date of review)	
<input type="checkbox"/> Review & Environmental Impact Statement (indicate date of each review)	

<p>NDA: Methods Validation</p>	<p><input checked="" type="checkbox"/> Completed <input type="checkbox"/> Requested <input type="checkbox"/> Not yet requested <input type="checkbox"/> Not needed</p>
<p>❖ Facilities Review/Inspection</p>	<p>NA</p>
<ul style="list-style-type: none"> • NDAs: Facilities inspections (include EER printout) <i>(date completed must be within 2 years of action date)</i> 	<p>Date completed: <input type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation</p>
<ul style="list-style-type: none"> • BLAs: <ul style="list-style-type: none"> ○ TBP-EER ○ Compliance Status Check (approvals only, both original and all supplemental applications except CBEs) <i>(date completed must be within 60 days prior to AP)</i> 	<p>Date completed: <input type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation Date completed: <input type="checkbox"/> Requested <input type="checkbox"/> Accepted <input type="checkbox"/> Hold</p>

Appendix A to Action Package Checklist

An NDA or NDA supplemental application is likely to be a 505(b)(2) application if:

- (1) It relies on published literature to meet any of the approval requirements, and the applicant does not have a written right of reference to the underlying data. If published literature is cited in the NDA but is not necessary for approval, the inclusion of such literature will not, in itself, make the application a 505(b)(2) application.
- (2) Or it relies for approval on the Agency's previous findings of safety and efficacy for a listed drug product and the applicant does not own or have right to reference the data supporting that approval.
- (3) Or it relies on what is "generally known" or "scientifically accepted" about a class of products to support the safety or effectiveness of the particular drug for which the applicant is seeking approval. (Note, however, that this does not mean *any* reference to general information or knowledge (e.g., about disease etiology, support for particular endpoints, methods of analysis) causes the application to be a 505(b)(2) application.)

Types of products for which 505(b)(2) applications are likely to be submitted include: fixed-dose combination drug products (e.g., heart drug and diuretic (hydrochlorothiazide) combinations); OTC monograph deviations (see 21 CFR 330.11); new dosage forms; new indications; and, new salts.

An efficacy supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2).

An efficacy supplement is a 505(b)(1) supplement if the supplement contains all of the information needed to support the approval of the change proposed in the supplement. For example, if the supplemental application is for a new indication, the supplement is a 505(b)(1) if:

- (1) The applicant has conducted its own studies to support the new indication (or otherwise owns or has right of reference to the data/studies).
- (2) And no additional information beyond what is included in the supplement or was embodied in the finding of safety and effectiveness for the original application or previously approved supplements is needed to support the change. For example, this would likely be the case with respect to safety considerations if the dose(s) was/were the same as (or lower than) the original application.
- (3) And all other "criteria" are met (e.g., the applicant owns or has right of reference to the data relied upon for approval of the supplement, the application does not rely for approval on published literature based on data to which the applicant does not have a right of reference).

An efficacy supplement is a 505(b)(2) supplement if:

- (1) Approval of the change proposed in the supplemental application would require data beyond that needed to support our previous finding of safety and efficacy in the approval of the original application (or earlier supplement), and the applicant has not conducted all of its own studies for approval of the change, or obtained a right to reference studies it does not own. For example, if the change were for a new indication AND a higher dose, we would likely require clinical efficacy data and preclinical safety data to approve the higher dose. If the applicant provided the effectiveness data, but had to rely on a different listed drug, or a new aspect of a previously cited listed drug, to support the safety of the new dose, the supplement would be a 505(b)(2).
- (2) Or the applicant relies for approval of the supplement on published literature that is based on data that the applicant does not own or have a right to reference. If published literature is cited in the supplement but is not necessary for approval, the inclusion of such literature will not, in itself, make the supplement a 505(b)(2) supplement.
- (3) Or the applicant is relying upon any data they do not own or to which they do not have right of reference.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, consult with your ODE's ADRA.