Mid-Review-Cycle and Post-Complete Response Letter Meetings

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MID-REVIEW-CYCLE MEETING (MRCM) OUTLINE

- Goals of MRCM
- What this Means to Industry and FDA
- Overall Impact
- Industry & FDA Responsibilities
- What Can Industry Do to Assist

What is New?

GDUFA II Establishes a Pre-ANDA Program for Complex Generic Drug Products

Applicants granted a Product Development Meeting OR a Pre-submission Meeting have the option of a Mid-Review Cycle Meeting (MRCM)

Goals:

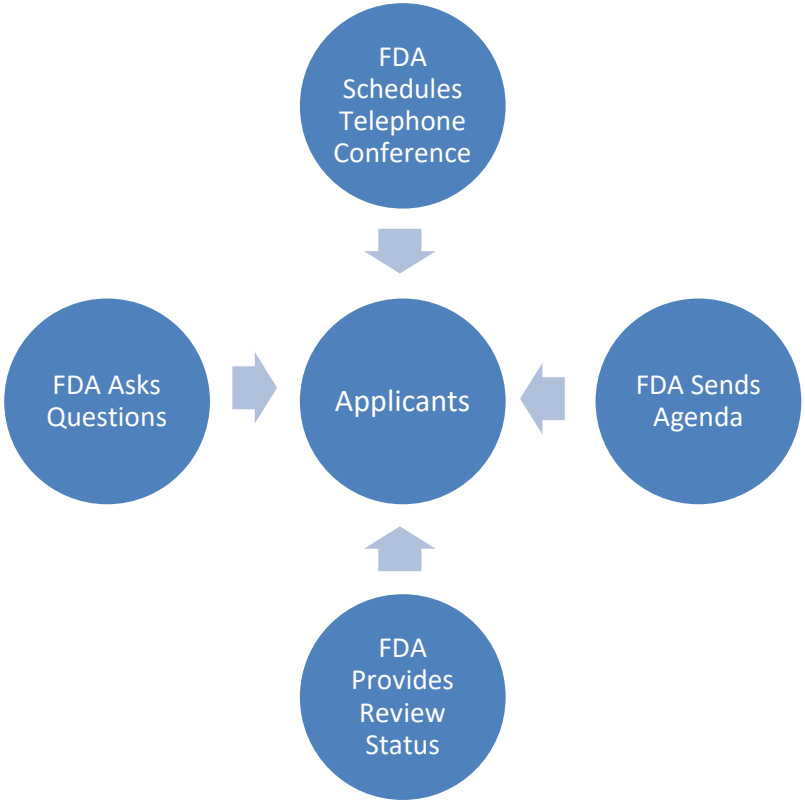
Clarify regulatory expectations in early development	Assist applicants with developing more complete submissions	More efficient/effective review process	Reduce # of cycles

MID-REVIEW-CYCLE MEETINGS ARE GENERALLY HELD FOR COMPLEX GENERIC DRUG PRODUCTS ONLY

Commitment Letter Language

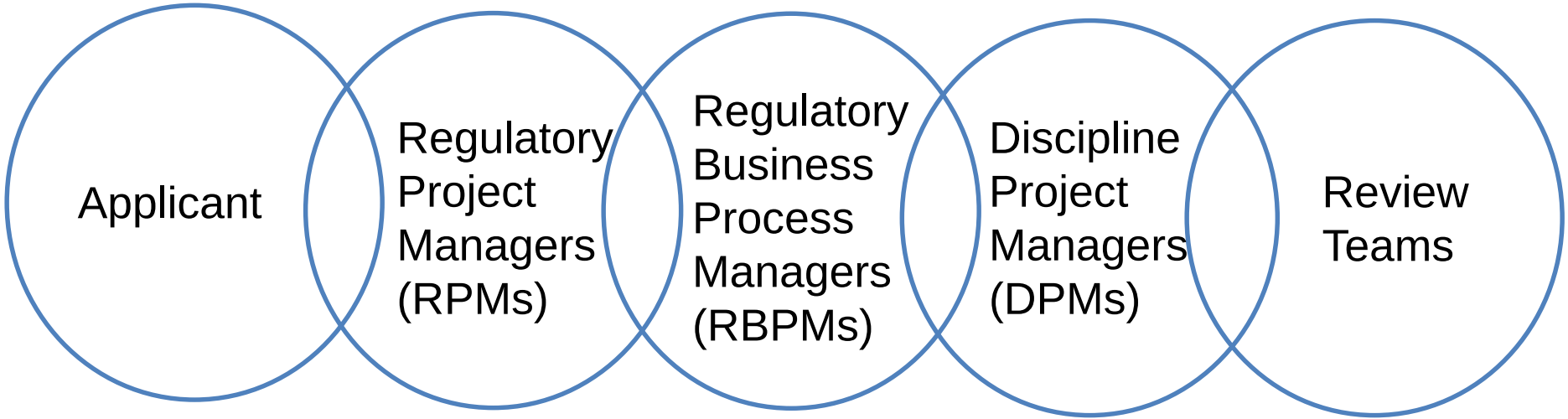
Section [III. F. 2.]: As set forth in guidance issued pursuant to Section III(A)(1), the Project Manager and other appropriate members of the FDA review team will call the applicant to provide the applicant with an update on the status of the review of their application. An agenda will be sent to the applicant prior to the mid-review-cycle meeting. The Project Manager will coordinate the specific date and time of the telephone call with the applicant.

What Does It Mean?

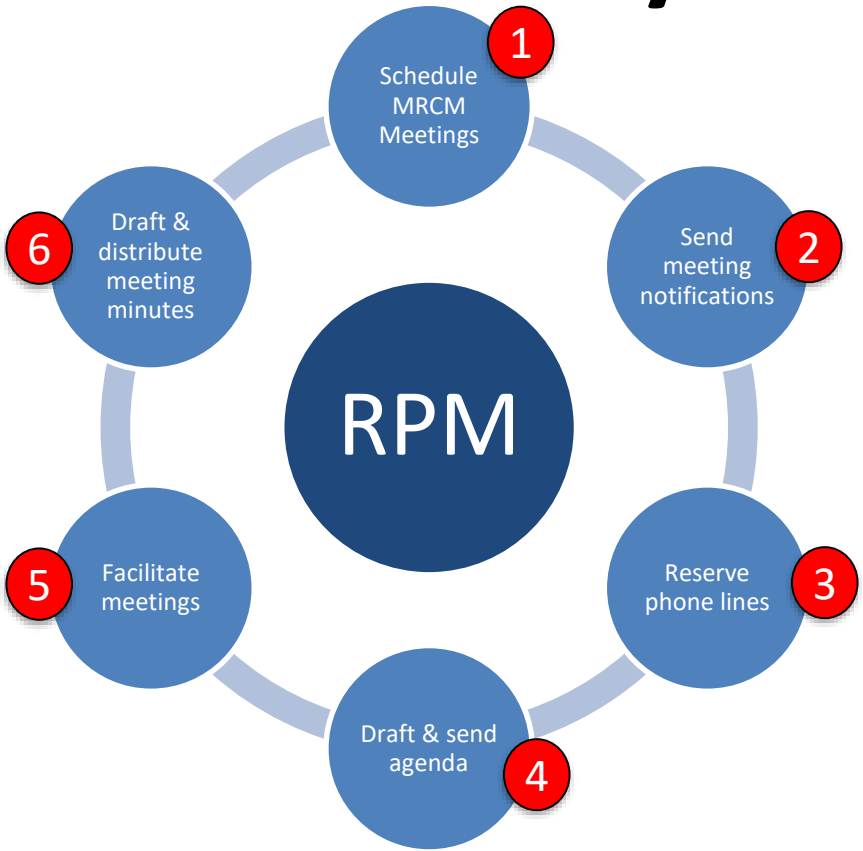


What is the Impact?

Who is Responsible?



What Will They Do?



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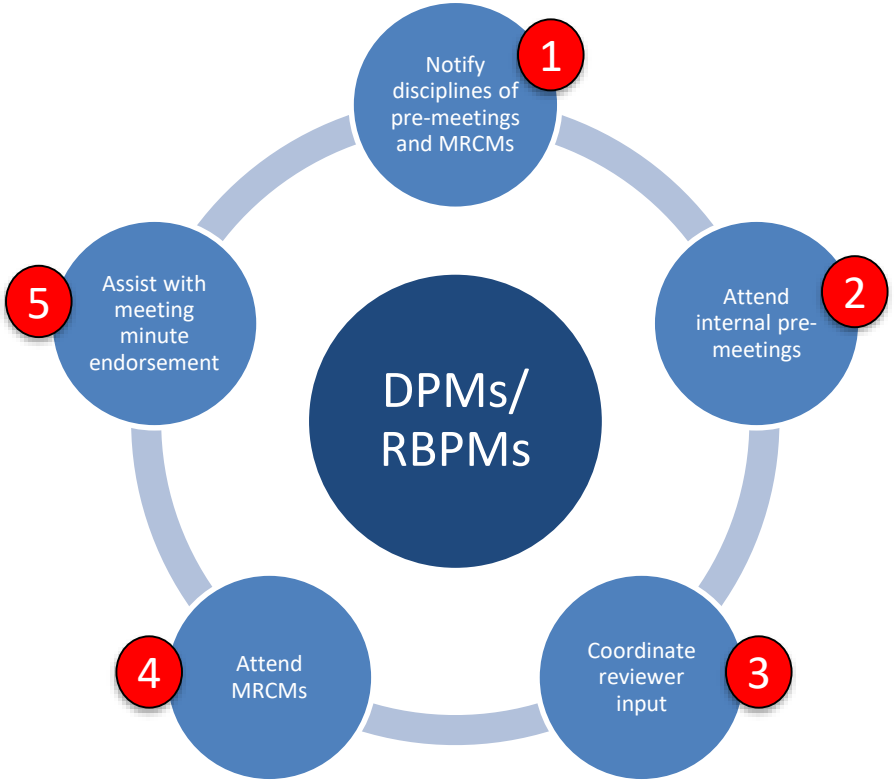


What Will They Do?

What Can Industry Do to Assist

Tips

- Clearly identify eligibility on cover letter
- Best to take first date suggested
- Have appropriate people attend meeting
- Not an opportunity for pre-review

For questions, please contact the Regulatory Project Manager assigned to the respective ANDA

U.S. FOOD & DRUG ADMINISTRATION

Post-Complete Response Letter Meeting Request (CRL MR) Tips

CRL MR Outline

- What is New/Changed?
- What Will Applicants/Agency Do
- What Should Industry Expect and Do
- Top Reasons Meetings are Denied
- Tips

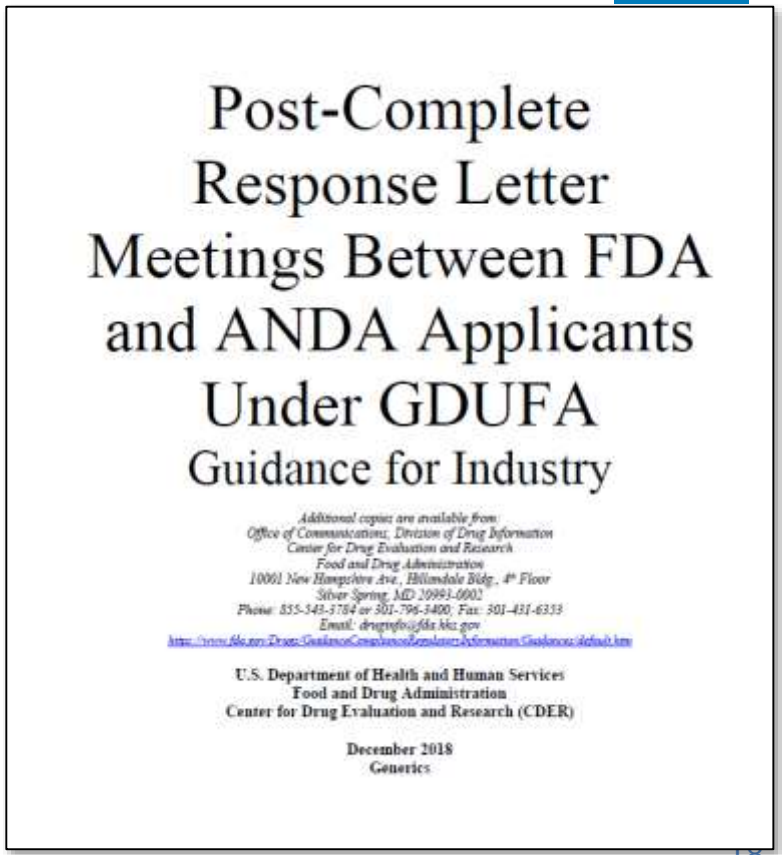
Commitment Letter Language

- II. Original ANDA Review Program Enhancements
  - B. ANDA Review Transparency and Communications Enhancements

    12. Applicants may opt for a post-CRL teleconference to seek clarification concerning deficiencies identified in a CRL. FDA will grant appropriate requests for teleconferences requested by applicants upon receiving first cycle major complete response letters. FDA will also grant appropriate requests for teleconferences requested by applicants upon receiving subsequent major complete response letters or minor complete response letters. FDA will provide a scheduled date for 90 percent of post-CRL teleconferences within 10 days of the request for a teleconference, and conduct 90 percent of such post-CRL teleconferences held on the FDA-proposed date, within 30 days of receipt of the written request.

Guidance for Industry

- GDUFA II goal dates
- Assessing CRL MR
  - Grant/deny criteria
  - Complete meeting packages
- Rescheduling/cancelling CRL MR
- Procedures for conducting CRL meeting teleconferences
- Documentation of meetings



Post-Complete Response Letter Meetings Between FDA and ANDA Applicants Under GDUFA

Guidance for Industry

Additional copies are available from:
Office of Communications, Division of Drug Information
Center for Drug Evaluation and Research
Food and Drug Administration
10001 New Hampshire Ave., Hillandale Bldg., 4th Floor
Silver Spring, MD 20993-0002
Phone: 855-543-3784 or 301-796-3400; Fax: 301-431-6353
Email: druginfo@fda.hhs.gov
http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

December 2018
Generics

Goal dates

- Provide a scheduled date for 90% of CRL MR within 10 calendar days of MR receipt

- Conduct 90% of CRL MR on FDA-proposed date within 30 calendar days of MR receipt

Calendar days

- Applicants have 10 calendar days to submit a CRL MR to be eligible for goal dates
- A CRL MR submitted after 10 calendar days will be granted if meeting request is otherwise complete but ineligible for goal dates

What Will Applicants Do?

- Applicant will submit a complete MR package within 10 calendar days of CRL issuance
  - List of proposed clarifying questions grouped by discipline
  - List of individuals from applicant's organization
  - Requested format of meeting
    - If teleconference, include proposed agenda outlining how the 30 minutes should be apportioned to each question
    - List of specific review disciplines

What Will the Agency Do?

Regulatory Project Manager

Project Managers for Quality or Labeling-only prior approval supplements (PAS)

- Identifies/triages/assigns MR
- Provides preliminary grant/deny decision
- Communicates with applicants and issues MR correspondence
- Schedules/facilitates teleconference
- Drafts meeting minutes
- Tracks goal dates

Review Team

Discipline Project Managers, RBPMs, Reviewers, Team Leaders, Division Directors

- Provides final grant/deny decision
- Provides responses to clarifying questions
- Attends teleconference
- Provides edits/concurrence to meeting minutes

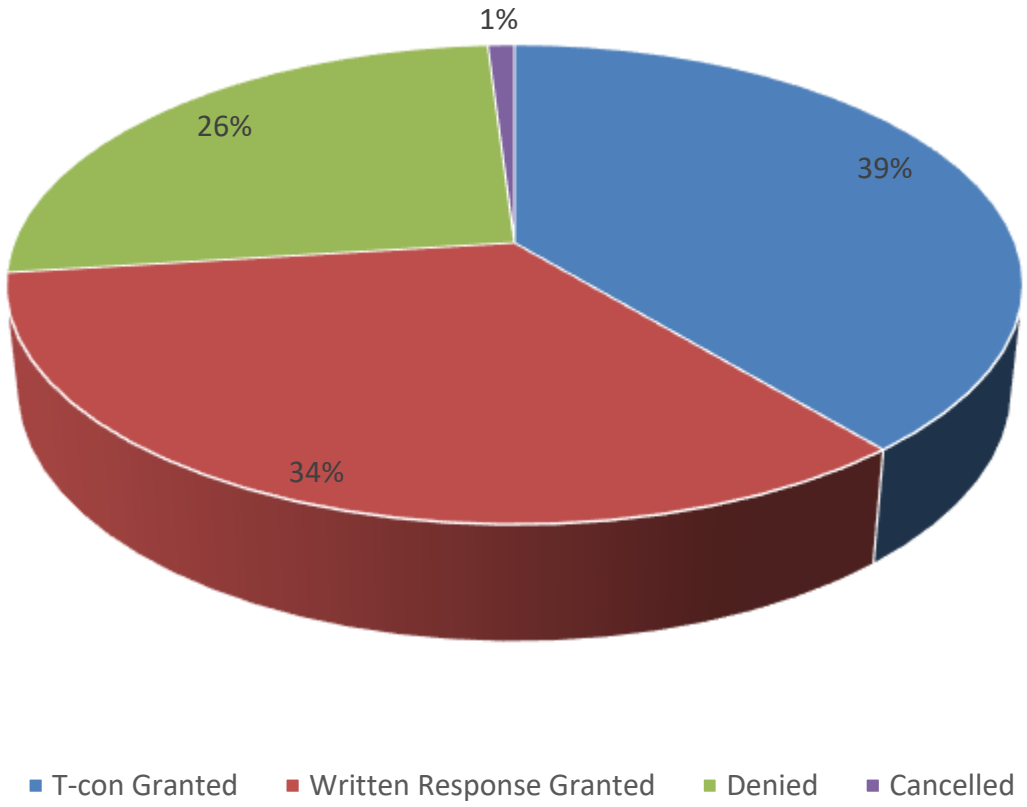
What Should Industry Expect?

- Predictable review times
- Timely communications
- Strict adherence to criteria for granting/denying meeting requests

What Can Industry Do to Assist?

- Submission of complete meeting package
- Clarifying questions only
- Courtesy email to RPM about forthcoming CRL MR

CRL MR Breakdown



Top Reasons Meetings are Denied

1. Non-clarifying questions
2. Questions outside scope of CRL deficiencies
3. Requests for Agency pre-review
4. Incomplete Meeting Request Package

Examples of Meeting Requests Denials

- Requests for Agency input on a testing method
- Requests for Agency input on study or formulation design
- Requests for amendment reclassification (major to minor)
- Proposals on how to address deficiencies in their CRL response
- Request not submitted after issuance of a CR
- Submission of a second post CRL meeting request in response to same CRL

Tips

- Email RPM courtesy copy of meeting request package and ensure it is complete
- Submit clear agenda outlining questions during the 30 minute meeting
- Prioritize topics for discussion
- Review FDA meeting minutes to ensure it reflects the meeting discussion

Tips for Industry

Post-CRL meeting requests are NOT …

- response or amendment pre-review
- pathway for request for reconsidera-tion or dispute
- consulting service

Resources

- **GDUFA II Commitment Letter:** GDUFA Reauthorization Performance Goals and Program Enhancements Fiscal Years 2018-2022

- **Guidance for Industry:** Post-Complete Response Letter Meetings Between FDA and ANDA Applicants Under GDUFA

External Contact

- OGD Regulatory Project Manager
  - Exceptions:
    - Labeling PAS: OGD Labeling Project Manager
    - Quality PAS: OPQ Regulatory Business Process Manager

OPQ Perspective for Post CR Meeting Requests

Ankara “Nikki” Yokum
Branch Chief
Division of Regulatory Business Process Management OPRO/OPQ

How is OPQ Involved for Original ANDAs?

- Meeting Requests involving Quality: OGD RPM will forward to the OPQ Regulatory Business Process Manager (RBPM)
- OPQ RBPM coordinates with Quality Assessment Team

OPQ Roles & Responsibilities

Quality Team (RBPM & Assessors) Responsibilities:

- Receive MR Package and Internal Deadlines from OGD
- Assess MR to determine if Grant/Deny
  - Provide Rationale if Denied
  - Prepare responses for meeting if granted
- Hold/attend internal quality meeting, as needed
- Attend teleconference (t-con)
- Assist with taking/editing official meeting minutes

OPQ Roles & Responsibilities

Regulatory Business Process Manager

- Triages/assigns MR to Quality Team
- Provides/tracks internal deadlines
- Relays grant/deny recommendation to OGD
- Schedules/facilitates internal quality meeting, as needed
- Attends teleconference (t-con)
- Assists with taking/editing meeting minutes

Quality Assessment Team

Primary, Secondary Assessors, ATL, Branch Chief(s), Division Director(s)

- Assesses meeting request package
- Provides grant/deny decision
- Attends Internal Meetings
- If denied, provides rationale
- If granted, provides responses to clarifying questions
- Attends/participates in t-con
- Provides edits/concurrence to meeting minutes

Examples: Reasons Meetings are Denied

- Non-clarifying questions/Requesting Pre-Review
  - Pre-review of new study design
  - Impurity limit
  - Facility Remediation Plan
- Proprietary questions without appropriate representation (i.e. DMF)
- Questions outside scope of CRL deficiencies
  - General advice on a change you are considering making and the impact (Ex: withdrawing a facility and replacing data with new one)
  - Asking the Agency to expedite review of the response to the CR letter

Examples: Meeting Requests Denied

- Disputing Deficiencies or Requesting for Reconsideration of the CR Letter
  - Requests for amendment reclassification (major to minor)
  - Often for facilities
- Request for Reconsideration Resources
  - ANDA Submissions-Amendments to Abbreviated New Drug Applications Under GDUFA
  - Requests for Reconsideration at the Division Level under GDUFA (Draft)

DMF Post CR Meeting Requests

- **From GDUFA II Commitment Letter**
  - FDA will grant and conduct teleconferences when requested to clarify deficiencies in first cycle DMF deficiency letters.
  - DMF holders must request such teleconferences in writing within 20 business days of issuance of the first cycle DMF deficiency letter, identifying specific issues to be addressed. FDA may initially provide a written response to the request for clarification, but if the DMF holder indicates that a teleconference is still desired, FDA will schedule the teleconference.
  - FDA will strive to grant such teleconferences within 30 days, giving priority to DMFs based on the priority of the referencing ANDA.
  - In lieu of a teleconference, the DMF holder may submit a request for an email exchange between FDA and the DMF holder. The request must identify specific issues to be addressed. After FDA responds to the request, the DMF holder may submit, and FDA will respond to, one follow up email to obtain additional clarification.

DMF Post CR Meeting Requests:

Tips:

- For first cycle teleconferences, submit to the electronic submission gateway (ESG)
- When in doubt, reach out to the DMFOGD@fda.hhs.gov email and the RBPM that issued the DMF deficiency letter

Instructions are on the DMF CR Template:

You may request a 30-minute teleconference for first cycle letters to discuss the contents of the letter. The written request should be submitted through the Electronic Submissions Gateway (ESG) within 20 business days of receiving this letter. Please also send a notification e-mail to DMFOGD@fda.hhs.gov and carbon copy the Regulatory Business Process Manager (RBPM) listed above.

In lieu of a teleconference, you have the option of submitting your questions regarding this letter by e-mail. Submit the request for an e-mail exchange within 20 business days to DMFOGD@fda.hhs.gov and carbon copy the RBPM listed above. The subject field of the e-mail should include the DMF number and "Request for E-mail Exchange". The e-mail should include the date of the letter and repeat the deficiency item(s) as received from FDA followed by your specific questions for each item.

FDA will grant one follow up e-mail if additional clarification is needed based on our initial e-mail response. Submit the request for a follow up e-mail to DMFOGD@fda.hhs.gov and carbon copy the RBPM listed above. The subject field of the e-mail should include the DMF number and "Request for E-mail Exchange Follow Up". The e-mail should include the date of the letter and the specific questions for follow up. FDA will strive to grant teleconferences or respond to e-mail exchange requests within 30 days, giving priority to DMFs based on the priority of the referencing ANDA. If you do not have a secure e-mail address, we will fax the responses to your request for e-mail exchange to the fax number on file for the DMF.

OPQ Tips

- Follow the criteria of the Post CR guidance
  - For questions of quality items outside of the CR letter, contact RBPM
- Send your clarification questions through the Meeting Request route instead of emailing the RBPM/RPM
- Have the right people on the call to facilitate discussion
- Stick to the agenda, save time to summarize your understanding
- Review FDA's meeting minutes (official copy)
- In CR response, reference post-CR meeting decisions or clarifications with your deficiency response(s)

Points of Contact

- Post CR ANDA Meetings
  - OGD RPM
  - Quality only PAS= OPQ RBPM
  - Labeling only PAS= Labeling PM
- IR/DRL
  - Discipline PM or RBPM that issued the letter
- DMF Post CR Meetings
  - RBPM, DMFOGD@fda.hhs.gov
- Questions for OPQ outside of the CR Letter Scope, including Post Marketing: CDER-OPQ-Inquiries@fda.hhs.gov.

Resources

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