OFFICE OF PHARMACEUTICAL SCIENCE

Management of the Complex Drug Substances Coordinating Committee

CONTENTS

PURPOSE

- This MAPP describes the roles and responsibilities of the Complex Drug Substances Coordinating Committee (CDS CC) in the Center for Drug Evaluation and Research (CDER), the procedures to be used for establishing CDS CC technical committees and working groups, the structure and function of technical committees and working groups, and the procedures to be used in designating members to serve.

BACKGROUND

- Policy for complex drug substances that are regulated by CDER has been the responsibility of several science and technical coordinating committees in CDER, including the Medical Policy Coordinating Committee (MPCC), the Pharmacology/Toxicology Coordinating Committee (PTCC), the Chemistry, Manufacturing, and Controls Coordinating Committee (CMC CC), and the Biopharmaceutics Coordinating Committee (BCC). To promote better communication and coordination internally and externally for complex drug substances, CDER established the Complex Drug Substances Coordinating Committee (CDS CC) in June 1998.

- Complex drug substances are active ingredients, excipients, and reagents with complex chemical structure, mixtures of chemical substances, and products produced by biotechnology, including the following:

Peptides	Proteins
Glycoproteins	Oligonucleotides
Naturally derived steroids	Thyroid extracts
Botanicals	Phospholipids

Oligo- and polysaccharides (excluding cellulose /starch as excipients)
Lipids (excluding simple fatty acids and their esters as excipients such as magnesium stearate)
Mixtures of naturally derived substances
Cell metabolites (usually small molecules) produced by recombinant DNA technology
Conjugates (complexes) of conventional drugs with macromolecules, such as monoclonal antibodies and lipids
Excipients (e.g., cyclodextran liposomal vesicles, biopolymer, microspheres, microbubbles)
Reagents (e.g., monoclonal antibodies, rDNA enzymes)
Other complex chemical substances regulated by CDER

- The purpose of the CDS CC is to provide advice on the following topics as they relate to complex drug substances:

1. Characterization, specifications, filing requirements, and other issues related to investigational new drug applications (INDs), new drug applications (NDAs), abbreviated new drug applications (ANDAs), and postapproval changes

2. Raw material controls, manufacturing process, process validation, and in-process controls

3. Final product characterization and release and shelf-life specifications

4. Batch-to-batch consistency

5. Pharmaceutical equivalence between a generic and the reference listed drug, including measures and their comparisons (equivalence intervals, confidence intervals, and criteria for comparisons) to ensure comparability (sameness) of the active ingredients

6. Chemical *sameness* under orphan drug regulations for determining exclusivity (considered upon request)

7. Clinical, clinical pharmacology, bioavailability and bioequivalence, or other technical issues with input from appropriate coordinating committees

REFERENCE

MAPP 7200.1 - Management of the Chemistry, Manufacturing, and Controls Coordinating Committee

ORGANIZATION

The following descriptions and explanations apply on a general basis. Specific implementation may be adjusted due to membership and workload on a case-by-case basis.

- **CDS CC**

1. **Oversight.** The Center Director will provide CDER oversight for CDS CC**.**

2. **Chairs**. The CDS CC chairs (one chair for Biopharmaceutics and one chair for Chemistry) are designated by the Director, Office of Pharmaceutical Science (OPS), and will include representation from the Office of New Drug Chemistry (ONDC).

3. **Executive Secretary/Project Manager.** The CDS CC chairs will designate an Executive Secretary, and/or Project Manager.

4. **Membership.** The CDS CC members include representatives named by ONDC, Office of Regulatory Policy, Office of New Drugs (OND), Office of Generic Drugs (OGD), and Office of Compliance. Representatives from the Medical Policy Coordinating Committee and its Clinical Pharmacology Section, the Pharmacology/Toxicology Coordinating Committee, and the Biopharmaceutics Coordinating Committee. Representatives from the Center for Biologics Evaluation and Research may also be invited to become members of CDS CC and its technical committees and working groups. As appropriate, representation will be requested from other FDA centers, Office of Regulatory Affairs, Office of Chief Counsel, and other units in the Agency.

5. **Alternates.** To provide for a broader base of involvement and to maintain the committee workflow, members unable to attend a particular meeting may designate an alternate to attend, provided the alternate is known to the committee chairs and will fully communicate the content of the discussion to the member.

6. **Observers.** Various units of the Agency with an interest in CDS CC topics may nominate observers to attend CDS CC meetings. The observers are approved by the CDS CC.

- **Technical Committees and Working Groups**

Technical committees are ongoing committees meeting on topics related to the main technical activities of the coordinating committee. Working groups are smaller, short-term ad hoc groups formed to address specific issues of concern to the coordinating committee.

1. **Chairs and Vice-Chairs.** The CDS CC will select a chair and vice-chair for each technical committee and working group, taking into account the individual's expertise, interest in the subject matter, and workload. As appropriate, two co-chairs may lead a technical committee. Each chair will serve for a 2-year term. When the chair's term expires, the vice-chair ordinarily is expected to become chair, with appointment of a new vice-chair. The CDS CC may determine that the chair's term should be extended, normally in 1-year increments. In general, there is no rotation of working group chairs because working groups are created for specific issues and the length of the projects is usually shorter than those undertaken by technical committees.

2. **Membership.** Membership on any technical committee or working group should usually be composed of four to six persons. Members are chosen to serve based on their qualifications, expertise, and interest in the subject matter. Members will usually serve a 3-year term, which may be extended when needed. The terms of the members should be staggered, as determined by the chair, so that no more than two members will be replaced each year. In general, there is no rotation of working group members. After formation of the working group, new members will be appointed by CDS CC to replace members lost by attrition or to bring additional expertise to the working group, as needed.

3. **Continuity of Technical Committees and Working Groups.** Generally, technical committees are maintained indefinitely, whereas working groups are short term, and are established on an ad hoc basis to address specific issues, and may report directly to CDS CC or through a technical committee, as appropriate. Once a working group's assignment is completed, the working group is disbanded.

RESPONSIBILITIES

- **CDS CC will respond to requests in the following areas:**

1. Providing information and advice to review divisions and OGD and ONDC staff during the review process for issues related to characterization, setting specifications, establishing raw materials and in-process controls, and making a recommendation on chemical *sameness* under the context of orphan drug exclusivity.

2. Providing quality control and assurance of consistency in the review of applications for complex drug substances, excipients, and reagents.

3. Providing support and/or assistance to OND and OGD review components receiving 505(b) and 505(j) applications for complex drug substances.

4. Developing comprehensive science and technical guidance for complex drug substances, excipients, and reagents, as appropriate.

5. Providing science and technical information and recommendations on complex drug substances, excipients, and reagents to the Director of CDER, CDER's Office of Regulatory Policy, and to others as necessary.

6. Working with CDER's Office of Testing and Research, including its Divisions of Product Quality Research and Pharmaceutical Analysis, the Product Quality Research Initiative (PQRI), and other intramural and extramural constituencies to generate information to support policy for complex drug substances, excipients, and reagents.

7. Working with the Advisory Committee for Pharmaceutical Science and other CDER and/or Agency advisory committees on science and technical issues related to complex drug substances, excipients, and reagents.

8. Working with the Center for Biologics Evaluation and Research's CMC CC on issues common to the two Centers.

- **The Executive Secretary/Project Manager will:**

1. Prepare the agenda for and summary minutes of each CDS CC meeting. Meeting minutes will be made available to CDS CC and research, policy, and review units as appropriate. Minutes will be filed on a shared drive under \CDS CC\meet\ YY-MM-DD.

2. Schedule CDS CC meetings and meetings on CDS CC-related issues in consultation with the chairs of CDS CC.

3. Maintain a current CDS CC membership list, organization chart, and the membership lists of all technical committees and working groups.

4. Provide project management of CDS CC efforts, including maintaining data on projected milestones, completion dates, and the current status of each project.

- **Technical Committees and Working Groups will:**

3. Serve as a source of advice and assistance to CDS CC in responding to CDER staff on matters pertaining to complex drug substances, excipients, and reagents.

3. Develop, as needed, policies and procedures, usually expressed as guidance for industry, guidance for reviewers, or MAPPs. Guidances will be developed in accordance with good guidance practices, using the current standard format (see MAPP 4000.2). Policies and procedures will be documented in the Manual of Policies and Procedures (see MAPP 4000.1).

3. Ensure that new policies and procedures developed by the technical committees and working groups of CDS CC adhere to the following general sequence:

    - Approval by the technical committee or the working group and its oversight technical committee (if there is one)

    - Approval by the CDS CC

    - Distribution to other CDER units, and other Center and Agency units, as appropriate, for comments

    - Approval by the technical committee or the working group and any oversight technical committee of the policies and procedures revised based on comments received

    - Final concurrence by CDS CC

    - Final concurrence by OPS

    - Final editing by appropriate staff

    - Submission to the Center Director and Office of Regulatory Policy for review, including OCC review, and publication. Although sign-off from all persons and/or units is not required, a clearance form that reflects their comments or concurrence should be prepared and forwarded to the chairs of CDS CC with the document.

4. Respond to questions from the pharmaceutical industry as submitted by the review units in the Center. All requests will be directed to the chairs of CDS CC through its Executive Secretary/Project Manager prior to a technical committee or working group initiating work on an issue to determine the most appropriate group to prepare a

response.

- **Chairs of Technical Committee and Working Groups will:**

  1. Schedule and conduct meetings of the technical committee or working group, as required, to fulfill the objectives assigned by CDS CC. The chair will prepare an agenda and distribute it to the members in advance of each meeting. The vice-chair will call and run meetings in the absence of the chairperson.

  2. Prepare brief minutes of each meeting. Minutes will be filed on the shared drive under the CDS CC directory. Further distribution of the minutes will be at the discretion of CDS CC.

  3. Ensure that copies of all records and deliberations are retained appropriately.

  4. Report to the CDS CC semiannually or as requested on the activities of the technical committee or working group. The chair should provide to the CDS CC Executive Secretary a summary of achievements since the last report to the CDS CC, a projection of activities for the next 6 months, and a list of any issues for which CDS CC input is needed.

- **Members of Technical Committees or Working Groups will:**

  1. Regularly attend the meetings of their groups.

  2. Actively participate in the work being done and the discussions in meetings. This may include researching additional information to bring to the technical committee or working group.

PROCEDURES

- **Creation of New Technical Committees or Working Groups**

  1. With concurrence and/or direction by CDS CC, a new technical committee or working group may be formed. Any individual who identifies such a need can make a request for a new technical committee or working group in writing to the chairs of CDS CC.

  2. A statement of the proposed objective of the technical committee or working group should include suggestions for names of persons to chair and serve on the group, the expected frequency of meetings, and time frame for completion of tasks.

  3. The CDS CC will determine whether the technical committee or working group

should be established. The CDS CC Executive Secretary/Project Manager will maintain a list of current technical committees and working groups and their respective members.

- **Disbandment of Technical Committees or Working Groups**

1. CDS CC will disband a technical committee or a working group if:

   - It reaches the end of its scheduled lifetime.

   - It has fulfilled its objectives.

   - The CDS CC determines the working group is not fulfilling a necessary function in the Center.

2. At least once a year, the CDS CC will review the list of technical committees and working groups to determine whether any of the groups should be disbanded or reactivated. If, after discussions with the chair, it appears that a group no longer performs a useful function, the CDS CC will issue a notice that the group has been disbanded. A copy of this notice will be filed in the appropriate subdirectory on the Center shared drive with the title "FINAL."

3. Approximately once a month, the CDS CC chairs will meet with the CDS CC Executive Secretary/Project Manager to discuss the status of CDS CC projects.

- **Communications With the Center and Other Affected Constituencies**

The activities of the CDS CC will be communicated to the Center and other affected constituencies through distribution and electronic filing of the minutes of the CDS CC and technical committee or working group meetings, through written guidances, formal training sessions, written opinions, or other means deemed appropriate.

EFFECTIVE DATE

This MAPP is effective on the date of publication.