POLICY AND PROCEDURES

OFFICE OF PHARMACEUTICAL QUALITY

Responsibility in OPQ for the Integrated Quality Assessment of Products Containing Drug Substances Composed of Amino Acid Polymers

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PURPOSE

This MAPP describes how the responsibility for the integrated quality assessment of products containing drug substances composed of amino acid polymers will be divided among the Office of New Drug Products (ONDP), the Office of Lifecycle Drug Products (OLDP), the Office of Process and Facilities (OPF), and the Office of Biotechnology Products (OBP) in the Office of Pharmaceutical Quality (OPQ).

- This MAPP serves as a guide for the Office of New Drugs (OND) and the OPQ Office of Program and Regulatory Operations (OPRO) to direct submissions and manage other interactions regarding the quality assessment of products containing drug substances composed of amino acid polymers.

- The procedures in this MAPP apply to the quality assessment performed by OPQ for all original investigational new drug applications (INDs), IND amendments, original new drug applications (NDAs), original biologics license applications (BLAs), NDA and BLA amendments, and supplements to approved NDAs and BLAs for products containing drug substances composed of amino acid polymers. This MAPP does not apply to abbreviated new drug applications. This MAPP does not apply to products containing amino acid polymers solely as excipients.

BACKGROUND

- Currently, OPQ sub-offices including ONDP, OLDP, OBP, and OPF perform product quality assessments for products ranging in size and complexity from small peptides to large glycoproteins. The manufacturing processes used by sponsors and applicants for these products include chemical synthesis, purification from a biological source, and biotechnology. This MAPP describes how responsibilities for the quality assessment of amino acid polymers will be divided among these offices within OPQ.

- The Biologics Price Competition and Innovation Act of 2009 changed the statutory authority under which certain protein products will be regulated by amending the definition of "biological product" in section 351(i) of the Public Health Service Act to include "a protein (except any chemically synthesized polypeptide)."[1]

- The assignment of responsibility for quality assessment as described in this MAPP does not represent an Agency determination of whether the product is or is not a "biological product" or whether the product will be regulated under the Federal Food, Drug, and Cosmetic Act or the Public Health Service Act.

POLICY

The following procedures and responsibilities apply to original INDs, IND amendments, original NDAs and BLAs, NDA and BLA amendments, and supplements to approved NDAs and BLAs:

- OPQ will divide the responsibilities for quality assessment of products containing drug substances composed of amino acid polymers among the sub-offices ONDP, OBP, OPF, and OLDP based on the size of the drug substance molecule (i.e., the number of amino acid residues) and whether it is manufactured entirely by chemical synthesis, or derived from a biological source, as summarized in Table 1 in the Attachment.

- For products containing drug substances that are mixtures, the component with the greatest number of amino acid residues and the manufacturing process used will be factors in determining the responsibility for quality assessment.

- OPQ sub-offices will consult each other when multiple offices have expertise that could contribute to the integrated quality assessment of these products, including review, inspectional and/or policy issues.

[1] Sections 7001-7003 of the Patient Protection and Affordable Care Act (Affordable Care Act) (Public Law 111-148).

- For combination products such as antibody-drug conjugates, where the responsibility for quality assessment of the amino acid polymer component falls under one office (e.g., OBP) and responsibility for assessment of the other component(s) falls under a different office (e.g., ONDP), the assessment will be a collaborative effort.

- For combination products consisting of two or more active ingredients that are amino acid polymers that separately fall under the responsibility of different offices, the quality assessment also will be a collaborative effort.

- OPQ sub-offices will address and resolve, if possible, any disputes concerning the responsibility for quality assessment of these products or, if a resolution cannot be obtained, the matter will be brought to the OPQ Office Director.

- OPQ will use established procedures and responsibilities for the implementation of this MAPP.

PROCEDURES AND RESPONSIBILITIES

INDs

For INDs, including amendments, submitted for products containing drug substances composed of amino acid polymers, OPRO will use the following to request assessor assignments, direct submissions, and manage other interactions regarding the responsibilities for the quality assessment of such products in OPQ:

- The responsibility for quality assessment of IND products containing drug substances composed of amino acid polymers is summarized in Table 1 in the Attachment.

- ONDP will perform the quality assessment of IND products containing drug substances composed of amino acid polymers that are:

  – ≤ 40 amino acids, regardless of how they are manufactured (whether made entirely by chemical synthesis, or derived from a biological source)
  – 41-99 amino acids, and made entirely by chemical synthesis

- OBP will perform the quality assessment of IND products containing drug substances composed of amino acid polymers that are:

  – 41-99 amino acids, and are derived from a biological source
  – ≥100 amino acids, regardless of how they are manufactured (whether made entirely by chemical synthesis, or derived from a biological source)

NDAs and BLAs

For original marketing applications for products containing drug substances composed of amino acid polymers, OPRO will use the following to request assessor assignments, direct submissions, and manage other interactions regarding the responsibilities for the quality assessment of such products in OPQ:

- The responsibility for quality assessment of original applications for products containing drug substances composed of amino acid polymers is summarized in Table 1 in the Attachment.

- ONDP and OPF will perform the quality assessment of original applications for products containing drug substances composed of amino acid polymers that are:

  – ≤ 40 amino acids, regardless of how they are manufactured (whether made entirely by chemical synthesis, or derived from a biological source)
  – 41-99 amino acids, and made entirely by chemical synthesis

- OBP and OPF will perform the quality assessment of original applications for products containing drug substances composed of amino acid polymers that are:

  – 41-99 amino acids, and are derived from a biological source
  – ≥100 amino acids, regardless of how they are manufactured (whether made entirely by chemical synthesis, or derived from a biological source)

For supplements to approved applications:

- OLDP and OPF will perform the quality assessment of supplements for products containing drug substances composed of amino acid polymers that are:

  – ≤ 40 amino acids, regardless of how they are manufactured (whether made entirely by chemical synthesis, or derived from a biological source)
  – 41-99 amino acids, and made entirely by chemical synthesis

- OBP and OPF will perform the quality assessment of supplements for products containing drug substances composed of amino acid polymers that are:

  – 41-99 amino acids, and are derived from a biological source
  – ≥100 amino acids, regardless of how they are manufactured (whether made entirely by chemical synthesis, or derived from a biological source)

REFERENCES

- FDA guidance for industry *Good Review Management Principles and Practices for PDUFA Products*
- MAPP 4150.1 *Role and Procedures of the CDER Ombudsman*
- MAPP 4151.1 Rev. 1 *Scientific/Regulatory Dispute Resolution for Individuals Within a Management Chain*
- MAPP 4151.2 Rev. 1 *Resolution of Differing Professional Opinions: Review by Ad Hoc Panel and CDER Director*
- MAPP 4151.8 *Equal Voice: Discipline and Organizational Component Collaboration in Scientific and/or Regulatory Decisions*
- MAPP 6025.3 *Good Review Practice: Consultative Review of Drugs Regulated Within OND*

EFFECTIVE DATE

This MAPP is effective upon date of publication.

CHANGE CONTROL TABLE

Effective Date	Revision Number	Revisions
12/11/18	N/A	Initial

ATTACHMENT 1

Table 1: Quality Assessment Responsibility in OPQ for Products Containing Drug Substances Composed of Amino Acid Polymers

<table>
<tr><th>Size (number of amino acid residues)</th><th>Manufacturing Process</th><th>Responsibility</th></tr>
<tr><td>≤40</td><td>• Made entirely by chemical synthesis
• Derived from a biological source</td><td rowspan="3">ONDP for INDs

ONDP and OPF for original applications

OLDP and OPF for supplements to approved applications</td></tr>
<tr><td rowspan="2">41-99</td><td>• Made entirely by chemical synthesis</td></tr>
<tr><td>• Derived from a biological source</td><td rowspan="2">OBP for INDs

OBP and OPF for original applications and supplements to approved applications</td></tr>
<tr><td>≥100</td><td>• Derived from a biological source
• Made entirely by chemical synthesis</td></tr>
</table>