“The ANDA Review Pathway” An Introduction

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Generic Drug Forum 2017

Definition of a Generic Drug

A drug product that is comparable to a brand/ reference listed drug product in dosage form, strength, route of administration, quality and performance characteristics, and intended use.

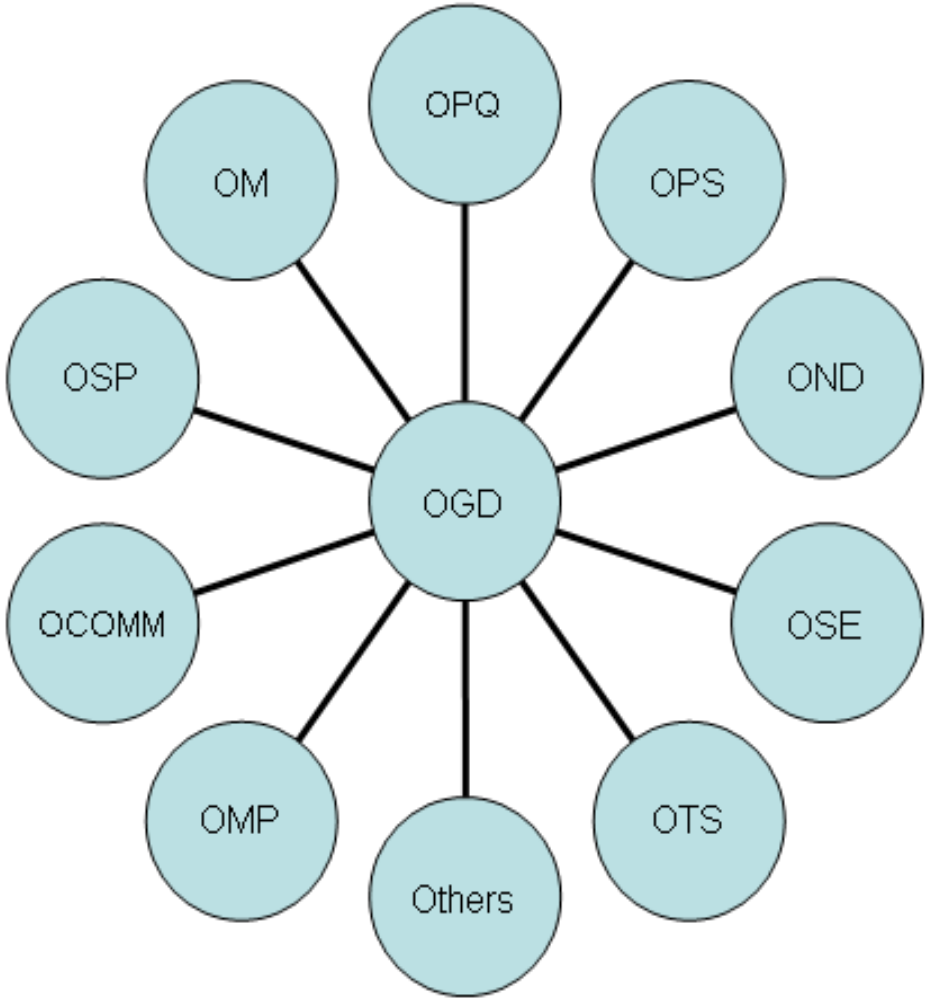
Generic Drug Requirements

- Same active ingredient(s)
- Same route of administration
- Same dosage form
- Same strength
- Same conditions of use
- Inactive ingredients already approved in a **similar** NDA

GENERIC DRUG PROGRAM

- Not just OGD
- All of CDER
- Other FDA units:
  - ORA
  - Office of the Commissioner
  - CBER, CDRH

- OGD is the interface for ANDA applicants to interact with the Generic Drug Program



Review Team

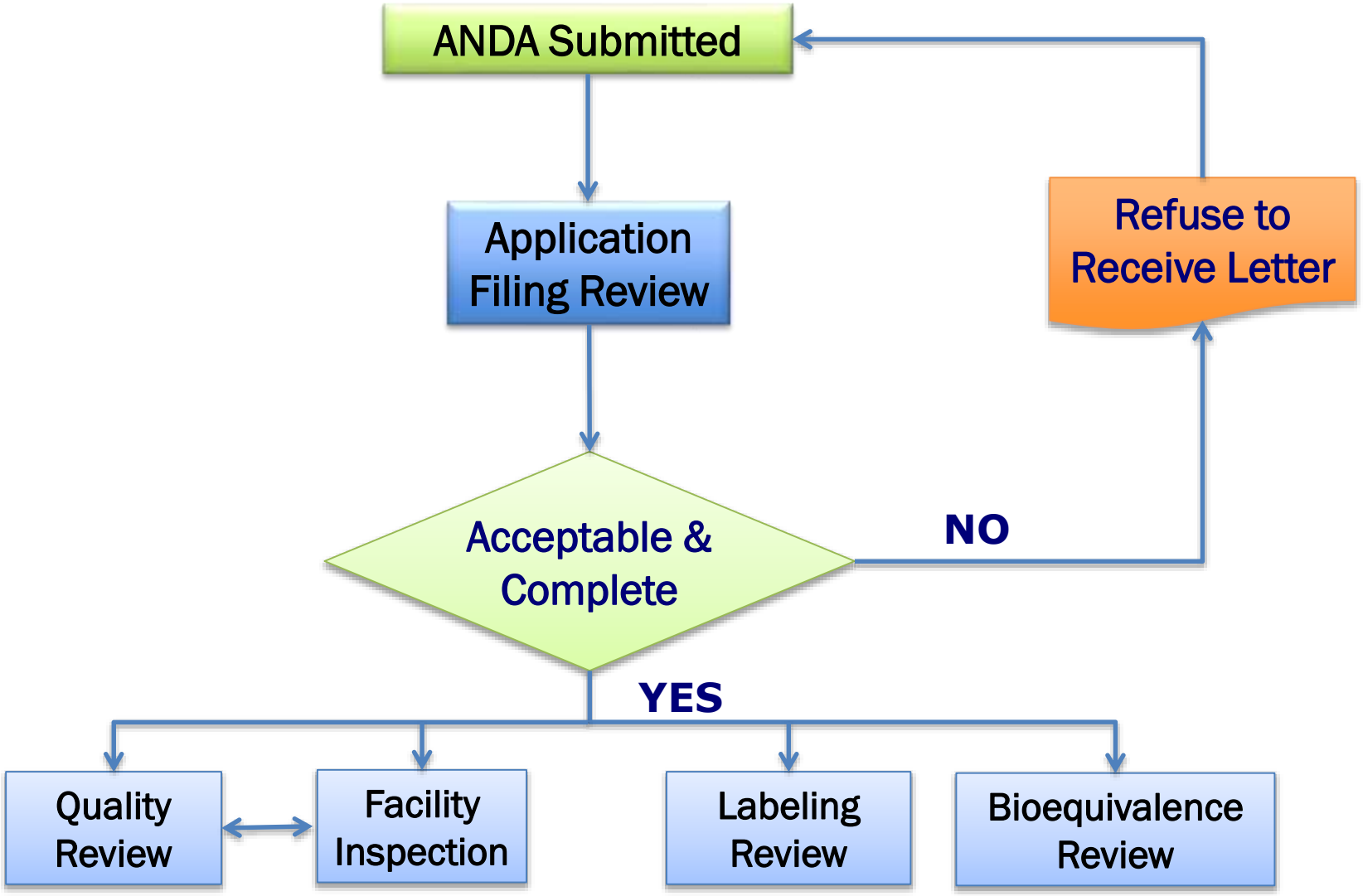
- Chemists
- Pharmacologists/Toxicologists
- Medical Officers/Clinicians
- Microbiologists
- Biopharmaceutists
- Statisticians
- Pharmacists
- Project Managers
- Support Staff

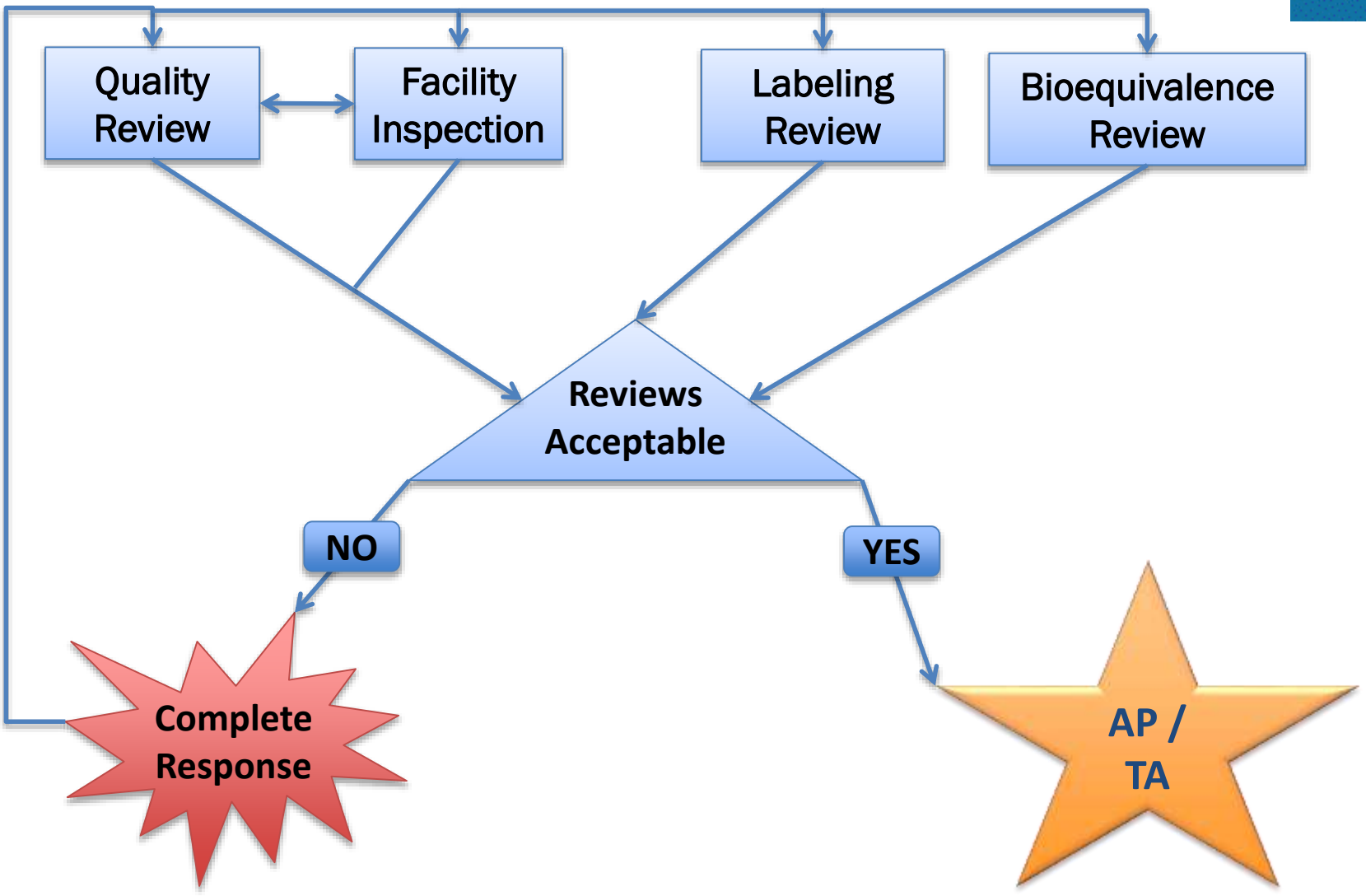
Key ANDA Review Questions

- Is the drug *as* safe and effective in it's proposed use(s)?
- Is the proposed labeling *matching the brand product's labeling*
- Are the methods used in manufacturing the drug and the controls adequate to assure *the same quality standards met*?
- *Is the generic substitutable to the brand?*

Brand Name Drug (NDA) Requirements	Generic Drug (ANDA) Requirements
1. Labeling	1. Labeling
2. Chemistry	2. Chemistry
3. Manufacturing	3. Manufacturing
4. Controls	4. Controls
5. Microbiology	5. Microbiology
6. Inspection	6. Inspection
7. Testing	7. Testing
8. Pharm/tox	8. Pharm/tox
9. Animal Studies	
10. Clinical Studies	9. Bioequivalence
11. Bioavailability	

Generic Drug Review Process




Quality Review
Facility Inspection
Labeling Review
Bioequivalence Review
Reviews Acceptable
NO
YES
Complete Response
AP / TA

Filing Review

- CTD Modules
  - Module 1 – Administrative
  - Module 2 – Summaries
    - 2.3 – Quality Overall Summary
    - 2.7 – Clinical Summary
  - Module 3 – Quality
  - Module 5 – Clinical Study Reports
- GDUFA Obligations Met (Filing Fee, Type II DMF Fee, and Facility Fee)
- DMF Complete Assessment (Complete/Incomplete)

Labeling Review

- “Same” as brand name labeling
- May delete portions of labeling protected by patent or exclusivity (i.e. an indication)
- May differ in excipients and product description (i.e. colors, shapes)

Quality Review

- Chemistry, Manufacturing and Controls
  - Components and composition
  - Manufacturing processes
  - Controls procedures
  - Batch formulation and records
  - Description of facilities
  - Specifications and testing
  - Packaging
  - Stability

Quality Review

- Microbiology
  - Assure the sterility of the product through the manufacturing process – especially important with injectable drug products

Inspection

- Verification of manufacturing and clinical sites
  - Assure adherence to and authenticity of data submitted in the application is being followed by the company
- Understanding of manufacturing
  - Assure manufacturing facilities are in compliance with current good manufacturing practices (CGMPs)
  - Assure bioequivalence sites are in compliance with current good clinical practices (CGCPs)

Testing

- Samples are collected from the companies' manufacturing facilities and are analyzed by ORA/Field laboratory
- Validation of manufacturing methods and case-by-case analysis and/or support by CDER labs

Pharm/Tox

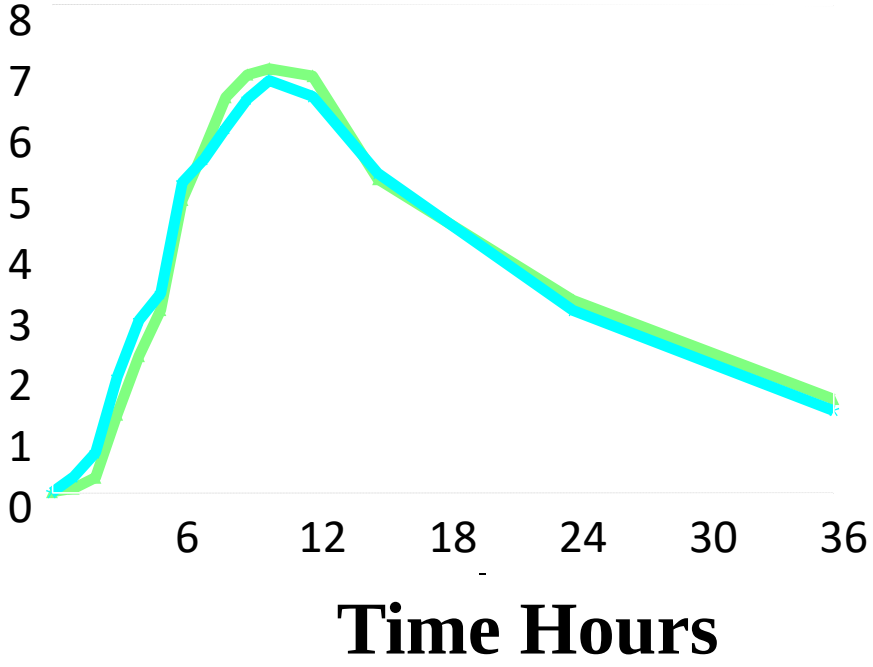
- All inactive ingredients must be approved in either the reference listed drug or similar NDA in same or higher levels. (FDA publishes the ingredient and highest approved levels.)
- Generic focus – is there anything unique to using this ingredient in the proposed generic

Bioequivalence

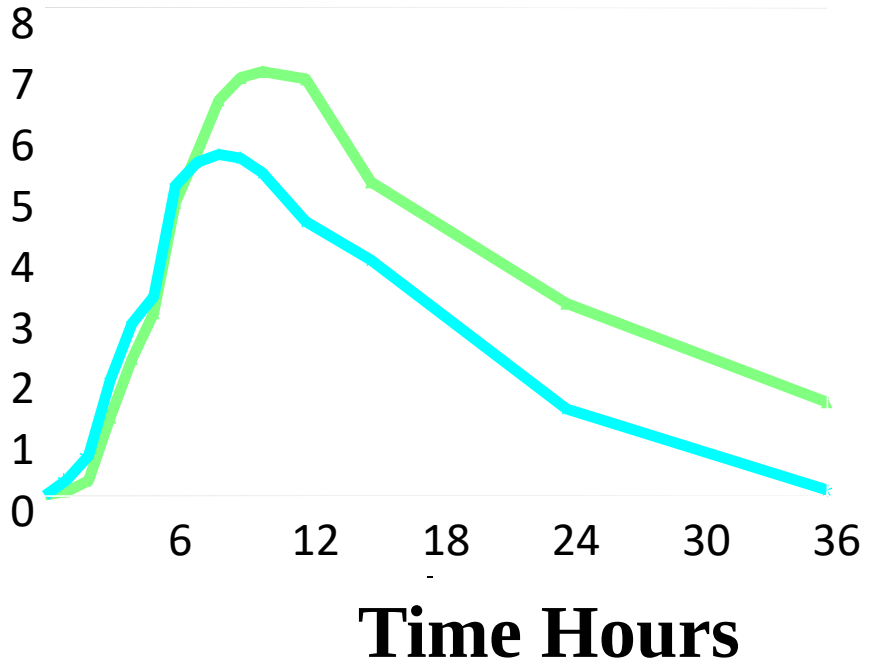
A generic drug is considered to be bioequivalent to the brand name drug if:

- The rate and extent of absorption do *not* show a significant difference from the listed drug, *or*
- The extent of absorption does *not* show a significant difference and any difference in rate is intentional or *not* medically significant

Bioequivalent



Inequivalent



- Test/Generic
- Reference/Brand

Regulatory Project Manager

- Oversee the review of ANDAs
  - Provide oversight across all review disciplines
  - Work to ensure all reviews are complete
  - Work to ensure OGD meets GDUFA goal dates
- Triage all amendments from receipt of ANDA to approval
  - Assign received amendments to the applicable disciplines
- Communicate key events in the approval process
  - MAPP 5200.3 Rev. 1
- Serve as point of contact
  - All communications will go through RPM
  - Exception: responding directly, as requested by a discipline

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Regulatory Actions

- **Refuse to Receive** – rejection of application due to problems or omissions resulting in an ANDA that is not substantially complete. Applicant can correct and resend.
- **Complete Response Letter** – communication describing all deficiencies identified during review.
- **Tentative Approval** – ANDA is ready for approval but cannot be approved due a patent or exclusivity related to the reference listed drug product
- **Approval** – ANDA product can be marketed

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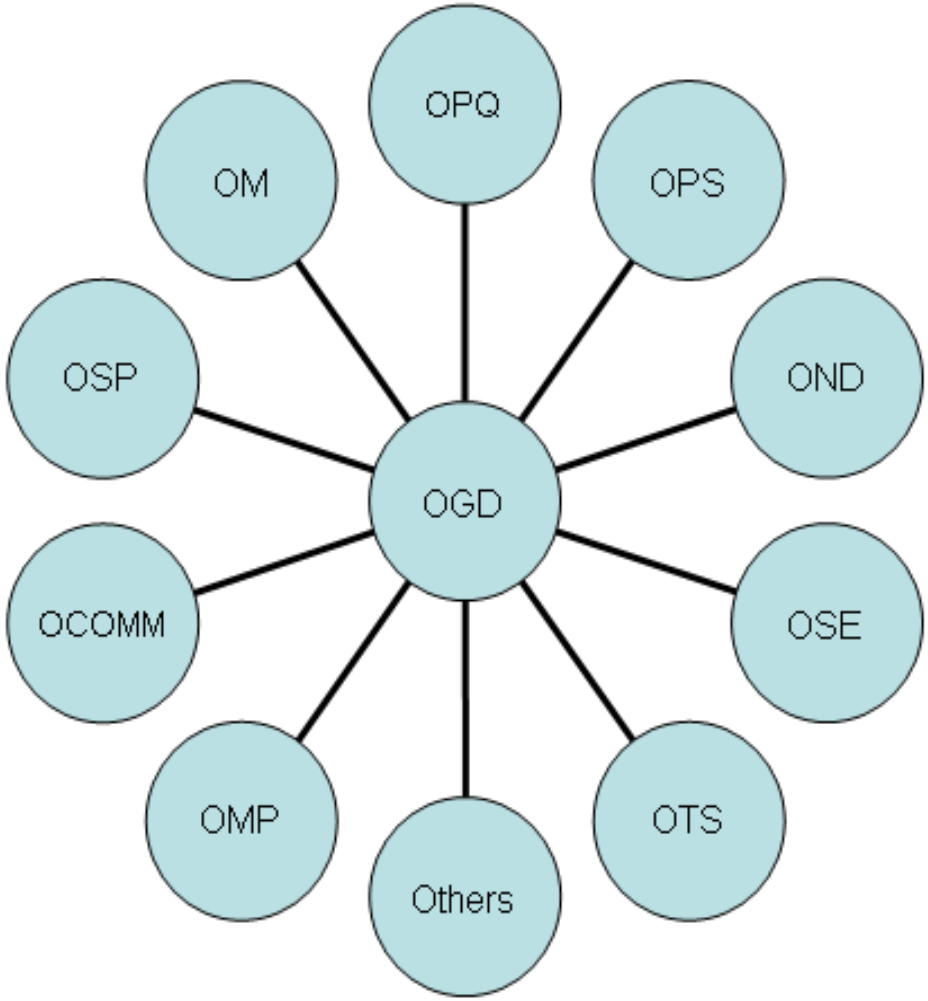

Thank You!

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