CBER/FDA Pharmacological Classification-Rationale

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Introduction

• Structured Product Labeling (SPL) is a document markup standard that defines the content of human drug product labeling in an XML (Extensible Markup Language) format. OD/CBER adopted SPL as a mechanism for exchanging medication information of approved biological products.

• The goal of this project is to index all CBER approved product labels with scientifically valid and clinically meaningful pharmacologic classification concepts, and make this information available on labels.fda.gov and the National Library of Medicine’s DailyMed website to improve search functionality across health care systems.

• The Established Pharmacologic Classes can assist health care professionals with important information on what they will generally know about a drug and how the drug might relate to other therapeutic options. Such information can also help reduce the risk of duplicative therapy and drug interactions, as well as provide important treatment information in cases of drug product overdose.
# Pharm Class Statistics

<table>
<thead>
<tr>
<th>Product Category</th>
<th>Number of Products</th>
<th>Number of new active moieties</th>
<th>Number of EPCs</th>
<th>Number of PEs</th>
<th>Number of MoA</th>
<th>Number of C/S</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccine</td>
<td>74</td>
<td>104%</td>
<td>33</td>
<td>3</td>
<td>0</td>
<td>33</td>
</tr>
<tr>
<td>Blood Derivatives</td>
<td>123</td>
<td>85%</td>
<td>40</td>
<td>11</td>
<td>8</td>
<td>28</td>
</tr>
<tr>
<td>Cell Therapy and Gene Therapy</td>
<td>8</td>
<td>4%</td>
<td>4</td>
<td>2</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>Non-Standardized Allergenic Extract</td>
<td>~1000</td>
<td></td>
<td>18</td>
<td>3</td>
<td>0</td>
<td>21</td>
</tr>
<tr>
<td>Standardized Allergenic Extract</td>
<td>19</td>
<td>24%</td>
<td>6</td>
<td>3</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>2011 approvals</td>
<td>8</td>
<td>60%</td>
<td>5</td>
<td>2</td>
<td>0</td>
<td>12</td>
</tr>
<tr>
<td>2012 approvals</td>
<td>1</td>
<td>100%</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>1233</strong></td>
<td><strong>1550</strong></td>
<td><strong>107</strong></td>
<td><strong>26</strong></td>
<td><strong>8</strong></td>
<td><strong>111</strong></td>
</tr>
</tbody>
</table>
An established pharmacologic class is represented by a term or phrase that is scientifically valid and clinically meaningful, the same as PE and MoA.

An active moiety in a particular biological product

Chemical/Ingredient is to group at active moiety level

Chemical/Ingredient

Pharmacologic effect at the organ, system, or whole body level

Physiologic Effect

Pharmacologic action at the receptor, membrane, or tissue level

Mechanism of Action

Established pharmacologic class

Active Moiety

An active moiety in a particular biological product

Established pharmacologic class

EPC

CS

Chemical / Ingredient

Indexing

Indexing

Indexing

Pharmacological classification concepts:
General Rationale (cont.)

• A pharmacologic class is a group of drugs that share scientifically documented properties.

• What is the rationale to index pharmacologic class in a particular package insert?

For example,

• How to choose an Established Pharmacologic Class (EPC) for a specific active moiety?

  • First need to understand the functionality, mechanism and molecule structure of the active moiety from a particular biological product
  • Search for scientifically valid and clinically meaningful “terms” in:

    • “(Drug) is a (name of pharm class) indicated for (indication(s)).”

• If there is not enough information above, we need to search Package Insert for Section “Description” and “Section “Clinical Pharmacology”

• Sometimes, we need to search out for other sources such as PubMed or directly contact the manufacturers.
## Vaccine Pharmacological Classification

- Vaccine pharmacological classification groups CBER approved vaccine products (active moiety) by their EPC, PE, MoA and Chemical/Ingredient-an example, BioThrax (Anthrax vaccine)

<table>
<thead>
<tr>
<th>Active Moiety</th>
<th>FDA UNII</th>
<th>FDA Text Phrase</th>
<th>NDF-RT Concept</th>
<th>NDF-RT NUI</th>
<th>NDF-RT Concept Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>BACILLUS ANTHRACIS STRAIN V770-NP1-R ANTIGEN</td>
<td>8730I62848</td>
<td>live attenuated Bacillus anthracis vaccine</td>
<td>Live Attenuated Bacillus Anthracis Vaccine [EPC]</td>
<td>N0000183903</td>
<td>EPC</td>
</tr>
<tr>
<td>BACILLUS ANTHRACIS STRAIN V770-NP1-R ANTIGEN</td>
<td>8730I62848</td>
<td></td>
<td>Actively Acquired Immunity [PE]</td>
<td>N0000183364</td>
<td>PE</td>
</tr>
<tr>
<td>BACILLUS ANTHRACIS STRAIN V770-NP1-R ANTIGEN</td>
<td>8730I62848</td>
<td>[MoA] Omitted</td>
<td></td>
<td>N/A</td>
<td>MoA</td>
</tr>
<tr>
<td>BACILLUS ANTHRACIS STRAIN V770-NP1-R ANTIGEN</td>
<td>8730I62848</td>
<td>Vaccines, Attenuated [Chemical/Ingredient]</td>
<td></td>
<td>N0000170873</td>
<td>Chemical/Ingredient</td>
</tr>
<tr>
<td>BACILLUS ANTHRACIS STRAIN V770-NP1-R ANTIGEN</td>
<td>8730I62848</td>
<td>Anthrax Vaccines [Chemical/Ingredient]</td>
<td></td>
<td>N0000170890</td>
<td>Chemical/Ingredient</td>
</tr>
</tbody>
</table>
Vaccines have 3 EPC terms both scientifically valid and clinically meaningful

Scientifically valid: “Terms” are documented in scientific publications, MeSH, and empiric evidence

Clinically meaningful: Clinical doctors need to know whether a particular vaccine is live unattenuated, live attenuated, or inactivated before prescribing.
Inactivated xxx vaccine

Scientific valid and clinical meaningful are based on Manufacturer’s Good Manufacturing Practice (GMP) on both product and labeling

**Inactivated xxx vaccines**

- **Fractional**
  - **Protein-based**
    - **Toxoid**: Diphtheria, Tetanus, Anthrax
    - **Subunit**: Hepatitis B, Influenza, Acellular Pertussis, Human Papillomavirus
  - **Polysaccharide-based**
    - **-Pure**: Pneumococcal, Meningococcal, Salmonella Typhi (Vi)
    - **-Conjugate**: Haemophilus Influenzae type B, Pneumococcal, Meningococcal
  - **Viruses**: Polio, Hepatitis A, Rabies, Influenza
  - **Bacteria**: Pertussis, Typhoid, Cholera, Plague

**Whole**
Live attenuated vaccine

Scientific valid and clinical meaningful are based on Manufacturer’s Good Manufacturing Practice (GMP) on both product and labeling.
Live Unattenuated vaccines

Scientific valid and clinical meaningful are based on Manufacturer’s Good Manufacturing Practice (GMP) on both product and labeling.
Live Attenuated Bacillus Anthracis Vaccine [EPC]

Live attenuated=clinical meaningful Bacillus-Genus name; Anthracis-Species name=scientific valid

*BA vaccine contains no cells but culture supernatant

Rationale

MoA

- Omitted (PE is enough)

PE

- Actively Acquired Immunity (new)-HLGT

Chemical/Ingredient

- Vaccines, Attenuated (new)-HLGT
- Anthrax Vaccines (NDF-RT existing)
Reference for Active Immunity of PE

Immunity
  ▼ Innate Immunity

Adaptive Immunity
  ▼ Natural
    ▼ Passive (maternal)
    ▼ Active (Infection)
  ▼ Artificial
    ▼ Passive (antibody transfer)
    ▼ Active (immunization)

Cell mediated immunity
  ▼ Active immunity
    ▼ Humoral immunity
      ▼ Antibody
      ▼ Opsonins
      ▼ Bacteriolysins
      ▼ Complement
      ▼ Antigen-specific Cytotoxic T lymphocytes
      ▼ Phagocytes
      ▼ Natural Killer Cells
      ▼ Cytokines release in response to an antigen

HLGT
## Non-Standardized Allergenic Product Pharm Class

- The pharmacological classification groups active moieties in CBER-approved non-standardized allergenic products by their PE, MoA and/or CS

<table>
<thead>
<tr>
<th>CHERRY</th>
<th>BUC5I9595W</th>
<th>non-standardized food allergenic extract</th>
<th>Non-Standardized Food Allergenic Extract [EPC]</th>
<th>code needed</th>
<th>EPC</th>
<th>Vada/OD/CBER</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHERRY</td>
<td>BUC5I9595W</td>
<td>Increased Histamine Release [PE]</td>
<td>N0000175629</td>
<td>PE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CHERRY</td>
<td>BUC5I9595W</td>
<td>Cell-mediated Immunity [PE]</td>
<td>N0000184306</td>
<td>PE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CHERRY</td>
<td>BUC5I9595W</td>
<td>Omitted [MoA]</td>
<td>N/A</td>
<td>MoA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CHERRY</td>
<td>BUC5I9595W</td>
<td>Allergens [Chemical/Ingredient]</td>
<td>N0000171131</td>
<td>Chemical/Ingredient</td>
<td>Vada/OD/CBER</td>
<td></td>
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<tr>
<td>CHERRY</td>
<td>BUC5I9595W</td>
<td>Dietary Proteins [Chemical/Ingredient]</td>
<td>N0000007512</td>
<td>Chemical/Ingredient</td>
<td>Vada/OD/CBER</td>
<td></td>
</tr>
<tr>
<td>CHERRY</td>
<td>BUC5I9595W</td>
<td>Fruit Proteins [Chemical/Ingredient]</td>
<td>code needed</td>
<td>Chemical/Ingredient</td>
<td>Vada/OD/CBER</td>
<td></td>
</tr>
</tbody>
</table>
Mechanism Illustration of Anaphylaxis
Mechanism Illustration of Immunotherapy

IgG antibody
Acknowledgements

CAPT (ret.) Hess A. William
LT CoCo Tsai, PharmD MPH
Mr. Lonnie Smith
Randy Levin, MD
Frank Switzer, PhD
Robert Yetter, PhD
Christopher Joneckis, PhD
Lawrence Callahan, PhD
Paul C. Brown, PhD

Erlbaum Mark, MD
Randall Stewart, MD
Mike Lincoln, MD
Ms. Grace Clifford