Global Regulatory Landscape of Complex Generics

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Objectives

1. Evaluate in ten countries the regulatory landscape and availability of complex products that fell under the guidance of the US FDA and other regulatory agencies.
2. Describe complex products and classify pharmacopeial quality standards for 13 active pharmaceutical ingredients across seven countries.

Introduction

Regulatory agencies around the world recognize guidelines and requirements for generic manufacturers to follow in the development, testing, and labeling of their products to ensure they meet the same standards as the innovator. These guidelines are intended to provide a foundation for the US Food and Drug Administration (FDA) and other regulatory agencies to determine the need for extensive clinical trials. For most generics, small scale innovation and reevaluation have to be made to the design for demonstration of all usually following standardized procedures.

The need for more effective treatments, including topical and parenteral dosage forms alongside improved patient compliance, has led to the development of non-biological complex products (BNPs). The US Food and Drug Administration (FDA) has classified these products in two major categories of complex products (Complex Generics): multi-functional active pharmaceutical ingredients (APIs) formulations, dosage forms, routes of delivery, and drug combination therapies. Categorization and approval of generics (BNPs) of these types of complex products (Complex Generics) require studies and the result is in the best general guidelines for complex generics. To address the additional studies required for approval, and guide manufacturers through the challenges in development, the US FDA publishes Product Specific Guidelines (PSGs).

Similarly, the European Medicines Agency (EMA) also recognizes that additional in vivo studies – beyond reliance on innovation studies – are required for the development and approval of generic versions of certain products, which are classified as ‘chemical generics’.

Beyond the US, the FDA and EMA, all agencies’ websites from several countries in different regions, specific classification and/or approval guideline are available for generics of APIs. To expand and better understand the International regulatory landscape of APIs, a more in-depth study was performed in ten countries across Africa, Asia, Europe, and Latin America, and the findings are presented here.

Methods

Information was gathered during 2016 through primary research at regulatory agency websites, other publicly available regulatory documents, printed market databases, national and regional pharmacopeias, and personal interviews with relevant stakeholders.

Results

In this work, the term BNP is utilized as a broad designation for products that pose challenges in determining its complex innovation, including but not limited to the complex or chemical modifications in the product, and medicines that are in 'form'. NBPs serve as a model for the most common types of complex products, specifically complex products that are in the seven countries assessed.

The APIs were selected based on a variety of criteria, including market size, prevalence of products in the region, and availability of quality standards. Table 1 lists the total number of available quality standards for non-complex and complex products in the seven countries assessed.

Table 1. Table of quality standards for non-complex and complex products

<table>
<thead>
<tr>
<th>Country</th>
<th>Non-complex Products</th>
<th>Complex Products</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa</td>
<td>12</td>
<td>5</td>
</tr>
<tr>
<td>Asia</td>
<td>15</td>
<td>5</td>
</tr>
<tr>
<td>Europe</td>
<td>25</td>
<td>10</td>
</tr>
<tr>
<td>Latin America</td>
<td>20</td>
<td>10</td>
</tr>
</tbody>
</table>

The US Food and Drug Administration (FDA) and other regulatory agencies have established a list of non-complex APIs for regulatory approval. This list includes APIs that are not complex, as defined by the US FDA and other regulatory agencies.

Table 2. Table of APIs identified in seven assessed countries

<table>
<thead>
<tr>
<th>API</th>
<th>Country</th>
<th>Non-complex Products</th>
<th>Complex Products</th>
</tr>
</thead>
<tbody>
<tr>
<td>API 1</td>
<td>Africa</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>API 2</td>
<td>Asia</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>API 3</td>
<td>Europe</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>API 4</td>
<td>Latin America</td>
<td>7</td>
<td>3</td>
</tr>
</tbody>
</table>

Discussion

The US FDA and MAHB recognize that, due to the complexity of certain products, the development at the regional level must be more extensive than the development at the country level. The diagram illustrates the percentage of APIs for which these regulatory agencies have established the list of APIs, and the percentage of APIs that are not complex. The APIs are classified as non-complex and complex products based on the criteria established by the regulatory agencies. The percentage of APIs that are not complex varies across the regions, with the highest percentage of APIs being complex in Latin America and the lowest in Africa.

Key Findings

- Each region has a list of APIs identified for regulatory approval.
- Complex products are more prevalent in Latin America and the least prevalent in Africa.
- The percentage of APIs that are not complex varies across the regions, with the highest percentage of APIs being complex in Latin America and the lowest in Africa.

References


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