Background
Both the European Medicines Agency (EMA) and US Food and Drug Administration (FDA) have guidelines that apply to the development and implementation of patient-reported outcomes (PRO) measures, regardless of whether they are explicitly used as an endpoint in clinical trials. These guidelines provide the necessary regulatory framework for developers and sponsors to ensure PRO assessments are conducted in a consistent and appropriate manner.

Objectives
The primary objective of this paper is to review the Provenance & Peer Review: 2018/001 guidelines on the use of PRO measures in clinical studies. The paper aims to identify commonalities and differences between the EMA and FDA guidelines to help researchers and sponsors make informed decisions when including PRO measures.

Methods
A targeted search was conducted for recent (2010-2015) European and US medical guidelines in the conditions mentioned above. Information pertaining to PROs within these guidelines was extracted and compared. Attention was paid to similarities, differences, and gaps across these guidelines.

Results

Generic Pain and Analgesic Indications

- Both EMA and FDA guidelines emphasize the importance of measuring pain intensity and pain relief in chronic pain conditions.
- The EMA guidelines highlight the use of the Visual Analog Scale (VAS) as the primary tool for measuring pain intensity.
- The FDA guidelines also recommend the use of the VAS, but they emphasize the use of numeric rating scales (NRS) for assessing pain intensity.
- Both agencies recommend using patient-reported outcome measures for assessing pain relief, with the EMA guidelines stating that pain relief should be assessed using a numerical rating scale.

Table 1: Comparison of EMA and FDA Guidelines for the Assessment of Generic Pain and Analgesic Indications

<table>
<thead>
<tr>
<th>Category</th>
<th>EMA Guidelines</th>
<th>FDA Guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain Intensity</td>
<td>Visual Analog Scale (VAS)</td>
<td>Numeric Rating Scale (NRS)</td>
</tr>
<tr>
<td>Pain Relief</td>
<td>Numerical Rating Scale (NRS)</td>
<td>Numerical Rating Scale (NRS)</td>
</tr>
</tbody>
</table>

Migraine

- Both EMA and FDA guidelines recommend including measures of headache frequency and duration, as well as symptom-specific measures such as nausea and photophobia.
- The EMA guidelines mention the use of the Headache Impact Test (HIT) as a measure of headache-related disability. The FDA guidelines recommend the use of the Migraine Disability Assessment (MIDAS) questionnaire.

Table 2: Comparison of EMA and FDA Guidelines for the Assessment of Migraine

<table>
<thead>
<tr>
<th>Category</th>
<th>EMA Guidelines</th>
<th>FDA Guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache Frequency</td>
<td>Not specified</td>
<td>Not specified</td>
</tr>
<tr>
<td>Headache Duration</td>
<td>Not specified</td>
<td>Not specified</td>
</tr>
<tr>
<td>Symptom-Specific Measures</td>
<td>Headache Impact Test (HIT)</td>
<td>Migraine Disability Assessment (MIDAS)</td>
</tr>
</tbody>
</table>

Systemic Lupus Erythematosus

- Both EMA and FDA guidelines recommend including measures of disease activity and damage assessment.
- The EMA guidelines recommend the use of the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) and the British Isles Lupus Assessment Group (BILAG) system for assessing disease activity.
- The FDA guidelines recommend the use of the Disease Activity Index (DAI) and the SLE disease activity index (SLEDAI).

Table 3: Comparison of EMA and FDA Guidelines for the Assessment of Rheumatoid Arthritis

<table>
<thead>
<tr>
<th>Category</th>
<th>EMA Guidelines</th>
<th>FDA Guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease Activity</td>
<td>Systemic Lupus Erythematosus Disease Activity Index (SLEDAI)</td>
<td>Disease Activity Index (DAI)</td>
</tr>
<tr>
<td>Damage Index</td>
<td>British Isles Lupus Assessment Group (BILAG)</td>
<td>SLE Disease Activity Index (SLEDAI)</td>
</tr>
</tbody>
</table>

Conclusions

- The EMA and FDA guidelines consistently recommend the development and use of valid and reliable PRO measures across different diseases and emphasize the importance of measuring symptoms from the patient perspective. Within similarities between EMA and FDA guidelines, variations between guidelines highlight the need for sponsors to become familiar with and incorporate guidelines specific to their drug development process.
- Both guidelines emphasize the use of PRO measures in clinical trials to assess the impact of treatments on quality of life.

References


Footnotes

- The EMA is the European regulatory agency that assesses the safety, efficacy, and quality of medicinal products in the European Union.
- The FDA is the regulatory agency responsible for ensuring the safety and effectiveness of medications in the United States.
- The SLEDAI is a disease activity index used to measure the severity of SLE.
- The BILAG is a classification system used to assess the severity of SLE.
- The MIDAS is a questionnaire used to measure the impact of migraine on daily life.
- The VAS is a common tool used to measure pain intensity on a scale from 0 to 100.
- The NRS is a scale used to measure pain intensity on a numeric scale from 0 to 10.

Image: The image contains tables with data comparing EMA and FDA guidelines across different disease areas, highlighting the similarities and differences in PRO measure recommendations.