Update on defining artemisinin as starting material

Presented by Valérie FAILLAT-PROUX
Rapporteur of the working group

WHO/MMV Artemisinin Conference
11-13 October 2010
Antananarivo, Madagascar
Last year – Artemisinin Annual Conference – September 2009

One road to artemisinin

Two pathways for artemisinin:
- one for API
- one for Starting Material
Last year – Artemisinin Annual Conference – September 2009

ARTEMISININ

API

Int. Ph Monograph for API

Starting material

Int. Ph Monograph for non-API grade

Guidance on starting material + annex on artemisinin

13/10/2010 Update on defining artemisinin as starting material
Guidance project – step 1

**Sept 2009**
Information of the group responsible for the expert committee

**Oct 2009**
Group led by André Van Zyl (Head of production and control of specified starting material -Includes artesimisinin as annex but may apply to other substances

- R. Stringham (Clinton Foundation)
- I. Bathurst (MMV)
- V. Faillat-Proux (sanofi-aventis)

**Nov. 2009**
Skeleton draft guidance on production and control of specified starting material

**April-May 2010**
Consolidation of comments
Review in 2 informal consultations

**March-April 2010**
Circulation of the first draft for comments

**Jan – Feb 2010**
Drafting of the guidance by the group

13/10/2010 Update on defining artesimisinin as starting material
Guidance project - step 2

- Document focused only on artemisinin
- General document that may apply to other substances than artemisinin

Guidance strategy?
Guidance project – step 2

May-June 2010
Technical discussion and drafting new version focused on artemisinin only

August-Oct 2010
Circulation of revised draft for comments

18-22 October 2010
Presentation to the 45th WHO expert committee on specification for pharmaceutical preparations

6 13/10/2010 Update on defining artemisinin as starting material
Guideline for artemisinin as Starting Material in the production of antimalarial Active Pharmaceutical Ingredients (APIs)

- Introduction
  - General principles on starting material
  - General principles on artemisinin as starting material
- Characterization of artemisinin
  - Focused mainly on impurities data, as major quality concern
- Tests and specifications for artemisinin starting material
  
  Specifications are based on experience with artemether and artesunate. New artemisinin derivatives API will need to demonstrate the suitability of these specifications.
### Draft guidance - Requirements

<table>
<thead>
<tr>
<th></th>
<th>Starting material</th>
<th>API monograph (int. Ph)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Identity</strong></td>
<td>IR</td>
<td>IR (or TLC+chemical reaction)</td>
</tr>
<tr>
<td><strong>Heavy metals</strong></td>
<td>10 ppm</td>
<td>-</td>
</tr>
<tr>
<td><strong>LOD</strong></td>
<td>5.0 mg/g</td>
<td>5.0 mg/g</td>
</tr>
<tr>
<td><strong>Related substances</strong></td>
<td>9-epi-artemisinin ≤3.0%</td>
<td>One impurity ≤0.5%</td>
</tr>
<tr>
<td></td>
<td>Any other impurity ≤0.5%</td>
<td>Any other impurity ≤0.25%</td>
</tr>
<tr>
<td></td>
<td>Sum of impurities ≤5.0%</td>
<td>Sum of impurities ≤1.0%</td>
</tr>
<tr>
<td><strong>Assay</strong></td>
<td>95.0-102.0% (HPLC)</td>
<td>97.0-102.0% (HPLC)</td>
</tr>
<tr>
<td></td>
<td>98.0-102.0% (TLC)</td>
<td></td>
</tr>
</tbody>
</table>
Not in the tests and specifications required for a starting material (compared to API)

- **Melting range** (not more relevant due to the use of HPLC method recommended for related substances)
- **Specific optical rotation** (not more relevant due to the use of HPLC method recommended for related substances and may be different due to the potential level of impurities)
- **Sulfated ashes** (not relevant for a starting material)
CHECK BACK SOON
At the dawn of well defined standards
Thank you