EARLY SCIENTIFIC ADVICE FROM PAYERS ACROSS THE EU

3rd December 2015
Graham Foxon and Paul Craddy
Why seek early scientific advice from Payers?

To help manufacturers generate evidence which is relevant for the future evaluation of the product by HTA bodies

- Improved patient access
- Develop more robust payer relevant evidence
- Align expectations
- Reduced uncertainty
- Faster time to market
- Reduced costs (potentially)
What questions are typically asked by companies seeking early payer scientific advice?

### Clinical Trial Programme
- Study population and subgroups
- Position in treatment pathway
- Comparators
- Trial design (duration, dosing)
- Acceptability of endpoints and surrogate endpoints
- Patient Reported Outcomes – generic and disease-specific
- Statistic analysis (subgroups, stratification)

### Economic Evaluation
- Economic model design and approach
- Sources of data (observational studies, literature)
- Resource use and utility values
When is the right time to seek scientific advice?

- Advice should be sought before finalisation of registrations studies protocols (e.g. PIII or PIib protocols)
- The company should be willing to make changes to the protocol based on the payer feedback!
What options exist to get scientific advice from HTA bodies in Europe?

National
• HTA advice from national HTA body

Parallel scientific advice
• Advice from EMA and some HTA bodies on regulatory and HTA issues

Multi-HTA
• Cooperative advice from EU national HTA bodies
Option 1: National HTA bodies

National
• HTA advice from national HTA body

Parallel scientific advice
• Advice from EMA and some HTA bodies on regulatory and HTA issues

Multi-HTA
• Cooperative advice from EU national HTA bodies
A number of countries are offering early scientific advice with their national HTA bodies.
The NICE standard scientific advice process takes 18-20 weeks

**PROJECT INITIATION**
- Company request slot in programme
- NICE confirms timelines and sends checklist to determine eligibility for project
- NICE sends template contract
- Company signs contract

**PROJECT CORE**
- Company sends briefing book to NICE
- NICE confirms project size
- NICE invoices for initial fee
- NICE updates and circulates contract
- Clarification questions are sent from NICE
- Company respond to clarification questions

Within 7 weeks of briefing book

Advice report issued from NICE

7 weeks for medium projects
9 weeks for large projects

Approx. 11 weeks after receiving briefing book

Face to face meeting with company and NICE

**PROJECT COMPLETION**
- Company receive advice report from NICE
- Company has no questions (within 15 working days)
- NICE sends invoice for remaining fee
- Project complete

- Company has questions on report (within 15 working days)
- NICE answers questions (within 30 working days)

1 month before briefing book is submitted

Seeking Early scientific advice from EU payers

© 2014 Remap Consulting GmbH

8 16/12/2015
The G-BA early scientific advice process typically takes up to 10 weeks

- **Written protocol and formal advice report**

**8 weeks**

- **Advice meeting with company**
- **Discussion at the committee**
- **Processing of request**
- **Submission of request**

- **14 days**

- **Special form**
- **General information, questions, position of the company and substantiation by company**
- **Fees apply**

- **Check completeness of request**
- **Identification of potential comparators**
- **Identification of potential endpoints**
- **Structured, systematic literature search**
- **Evidence synthesis**

- **Formal advice**
- **Explanation and discussion of key themes**

- **Agreement on comparator**
- **Agreement on further question of the company**

- **Submission of request**
- **Processing of request**
- **Discussion at the committee**
- **Advice meeting with company**
- **Written protocol and formal advice report**

Seeking Early scientific advice from EU payers
Option 2: Parallel scientific advice

**National**
- HTA advice from national HTA body

**Parallel scientific advice**
- Advice from EMA and some HTA bodies on regulatory and HTA issues

**Multi-HTA**
- Cooperative advice from EU national HTA bodies
The EMA – HTA parallel scientific advice process takes ~ 26 weeks to complete

**Pre-notification**
- Initial informal interaction with EMA & HTA’s to notify them of the intent to proceed with the PSA
- Notification should include details of HTA bodies proposed, targeted timelines, whether a pre-validation meeting will be requested
- Must be sent at least 2 months in advance of the formal Letter of Intent (LoI)

**Pre-validation**
- LoI and common Briefing Book (BB), including questions, is submitted for validation check
- Opportunity for a TC with Regulators/HTAs to discuss the scope, wording and clarity of the questions, and whether the material provided is sufficient to answer the questions posed

**Meeting**
- A face-to-face meeting between all stakeholders will be scheduled.
- Meeting will last approximately four hours.
- Company is required to submit meeting minutes (within 5 days) to regulators and each HTA

**Outcome**
- A final EMA advice letter containing CHMP regulatory advice
- Individual HTA feedback (according to HTA national procedure or by annotating the Applicant’s minutes).
The briefing book is the reference document containing all the information and questions used within the joint PSA process.

**Briefing book – Table of contents**

- PRODUCT VALUE PROPOSITION
- BACKGROUND INFORMATION
- Disease to be Treated
- Indication
- Quality Information on the Product
- Drug Substance
- Drug Product
- Nonclinical Information
- Pharmacology
- Clinical Information
- Clinical Pharmacology
- Clinical Efficacy
- Clinical Safety
- Clinical Development
- Regulatory Status
- Economic Evaluation Plans
- QUESTIONS AND COMPANY’S POSITIONS
- LIST OF REFERENCES
Option 3: Multi HTA

National
• HTA advice from national HTA body

Parallel scientific advice
• Advice from EMA and some HTA bodies on regulatory and HTA issues

Multi-HTA
• Cooperative advice from EU national HTA bodies
Multi-HTA advice is currently in the pilot phase and is managed by EUnetHTA and the SEEDs consortium

- The aim is continuous improvement of early dialogues through EUnetHTA and SEED: Shaping European Early Dialogues for health technologies

**JA1**
- Two preparatory early dialogues
- ED procedure drafted for JA2

**JA2**
- Draft ED procedure in JA1 used for 8 ED pilots
- ED survey conducted after first 6 ED pilots
- Refined ED procedure following WPT FtF meeting (Jan14) based on discussion (taking into account survey results)

**SEED**
- Revised JA2 EUnetHTA ED procedure used as the basis for SEED
- ED procedure further amended (Nov 14) and progressively introduced with SEED’s 8th ED
- Conducted nine EDs to date (6 drugs/3 medical devices)
- 10th ED planned in March; additional 11th ED planned in June

**JA2**
- One ED ongoing (medical device in heart disease)
- Three additional EDs conducted; June and Sept 2015

**SEED**: Shaping European Early Dialogues for health technologies
Multi-HTA advice is a voluntary, confidential, process but the advice is non-binding!

Voluntary, not binding, confidential

Input from company

- Provides a structured submission file (Briefing book) containing:
  - Development strategy, description of planned studies
  - Prospective questions and company's position for each question relevant to the development plan
- Issues related to the relative effectiveness and/or economic aspects
- Questions to ask the HTA bodies
The Multi-HTA process aims to be completed within 100 days.
Some challenges ahead for the multi-HTA process

From a EU sponsored to a self-sustainable model
- How to collect fees at international level?
- SMEs, orphan drugs: fees waivers/fees reduction?

Choice of participating HTA bodies

Relatives roles of national vs international

Impact on HTA organisation, how to develop expertise

From product-specific to disease specific advice?

Link with advise on additional evidence generation (Adaptive pathways...)

Seeking Early scientific advice from EU payers

© 2014 Remap Consulting GmbH
Do seek early payer scientific advice – the benefits outweigh the risks

- Early payer scientific advice is aimed at securing reimbursement as well as regulatory approval from the company’s clinical development program
- Seeking payer advice is a time and resource intensive process – ensure that the company allocates relevant expertise throughout the process
- Ensure the company is prepared to act on the feedback from early payer scientific advice and adapt the clinical development plan accordingly
- All payer guidance is confidential, but the feedback is non-binding

<table>
<thead>
<tr>
<th>Criteria</th>
<th>National</th>
<th>Parallel</th>
<th>Multi-HTA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of HTAs</td>
<td>One</td>
<td>Up to 5 + EMA</td>
<td>14 (at the moment)</td>
</tr>
<tr>
<td>Feedback format</td>
<td>Individual country</td>
<td>Individual HTA/EMA</td>
<td>HTA consensus</td>
</tr>
<tr>
<td>EMA perspective</td>
<td>No</td>
<td>Yes</td>
<td>If requested</td>
</tr>
<tr>
<td>Cost</td>
<td>€10-50,000</td>
<td>~ €80,000</td>
<td>Free (moving to fee based funding)</td>
</tr>
</tbody>
</table>
THANK YOU

Paul Craddy
Paul@remapconsulting.com
+41 (0) 79 963 1059

Graham Foxon
Graham@remapconsulting.com
+44 (0) 741 594 6778