Managing uncertainty & benefit / risk over the life cycle of a medicine

A CALL FOR ADAPTABILITY & FLEXIBILITY IN PHARMACEUTICALS REGULATION FROM A PATIENT AND INDUSTRY VIEW

Tony Hoos, M4P

The acceptance of uncertainty and risk may be quite different....

- A mother who gets her healthy child vaccinated
- A patient who suffers from asthma and who lives a normal life
- A patient who suffers from thyroid cancer
- A patient who has a bolus obstructing his / her airway
What is an acceptable level of uncertainty and benefit / risk in context of the medical need and public health benefit?

One size does not fit all – adaptive approaches are needed
How much data do we need to offer a medicine to patients? How do we assess benefit / risk?

R&D Expenditure per employee 2000-2007
Industry comparison

- Biopharmaceuticals: $105,428
- Communications equipment: $62,995
- Semiconductors: $40,341
- Computers and electronics: $37,980
- Chemicals: $34,978
- Navigational, measuring .....: $22,262
- Aerospace products: $22,162
- Motor vehicles, trailers, parts: $15,704
- Transportation equipment: $15,963
- Petroleum, coal: $13,319
- All Manufacturing: $9,956
- Electrical equipment, appliances: $6,411
- Machinery: $5,663
- Paper, Printing: $2,238

Adapted from: www.manhattan-institute.org : Project FDA Report #5 – March 2012
The Patients’ view on the regulatory process

Table 7: Participant Perceptions about Regulatory Processes

<table>
<thead>
<tr>
<th>Current Perceptions</th>
<th>A ‘Fit for Purpose’ Regulatory System</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protects the public</td>
<td>Protects vulnerable patients</td>
</tr>
<tr>
<td>Too slow and bureaucratic</td>
<td>Quick and flexible</td>
</tr>
<tr>
<td>Set in its ways</td>
<td>Accountable</td>
</tr>
<tr>
<td>Rare disease patients are excluded and isolated</td>
<td>Considers rare diseases differently</td>
</tr>
<tr>
<td>Not transparent enough</td>
<td>Transparent</td>
</tr>
<tr>
<td>Paternalistic</td>
<td>Patients’ views are represented</td>
</tr>
<tr>
<td></td>
<td>Patients are given information, support and choice</td>
</tr>
</tbody>
</table>

Source: Genetic Alliance UK: New Medicines for Serious Conditions: How Patients would weight the risks and benefits – April 2014
A joint effort is needed to advance Adaptive regulation is one key part
The Patients' view – Engagement in Regulatory decision making
The Patients’ view on access to medicines

Figure 15: Circumstances in which Patients Should Be Allowed Access to Medicines (if they want)

Survey statements about the permissiveness of regulators

- ...that have been tested on fewer people than normal
- ...where it is uncertain how well the medicine will work
- ...sooner than normal – for example, before they have been through all of the clinical trial stages
- ...that cause more, possible serious, side effects than normal
- ...where there is a significant risk of death

Number of respondents

Source: Genetic Alliance UK: New Medicines for Serious Conditions: How Patients would weight the risks and benefits – April 2014
The Patients’ view on decision making

Table 12: Survey Respondents Views on Patient Involvement

<table>
<thead>
<tr>
<th>Q12-15</th>
<th>Setting the research agenda</th>
<th>Designing clinical trials</th>
<th>Marketing authorisation decisions</th>
<th>Post-marketing authorisation decisions</th>
</tr>
</thead>
<tbody>
<tr>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>Patient decides</td>
<td>10.1</td>
<td>7.8</td>
<td>10.1</td>
<td>10.3</td>
</tr>
<tr>
<td>Joint decision making</td>
<td>57.8</td>
<td>48.8</td>
<td>48.6</td>
<td>55.1</td>
</tr>
<tr>
<td>Involvement</td>
<td>18.9</td>
<td>27.2</td>
<td>23.0</td>
<td>19.8</td>
</tr>
<tr>
<td>Consult before deciding</td>
<td>13.2</td>
<td>16.3</td>
<td>18.3</td>
<td>14.8</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

Source: Genetic Alliance UK: New Medicines for Serious Conditions: How Patients would weight the risks and benefits – April 2014
Traditional vs. adaptive licensing

Current model of licensing
“The Magic Moment”

Adaptive Licensing

Knowledge, investment

Time (years)
Adaptive Licensing - What is it?

- AL is a **prospectively planned**, adaptive approach to regulation of drugs.

- Through iterative phases of evidence gathering followed by regulatory evaluation and license adaptation, AL seeks to balance timely access for patients with the need to provide adequate evolving information on benefits and harms.

- AL **builds on existing regulatory processes**, including Conditional Authorization and RMPs.

- To achieve the full potential of AL for public health and drug development, licensing decisions should be aligned with coverage and prescribers’ decisions.

- AL is **not** about ‘cutting corners’, etc..!!

Modified from: G Eichler et al., Adaptive Licensing: Taking the Next Step in the Evolution of Drug Approval, Clinical Pharmacology & Therapeutics (2011); 91 3
Adaptive Licensing – Principles
prospective management & reduction of uncertainty
continuous assessment of benefit / risk

- Drug evaluation as a continuum
- Stakeholders need to agree on acceptable level of risk/uncertainty
March 2012: Multi-Stakeholder Thought Leadership

Adaptive Licensing: Taking the Next Step in the Evolution of Drug Approval

H-G Eichler1,2, K Oye3,4, LG Baird2, E Abadie5, J Brown6, CL Drum7, J Ferguson7, S Garmer8,9, P Honig10, M Hukkelhoven11, J CW Lim12, R Lima13, MM Lumpkin14, G Neil15, B O’Rourke16, E Pezalla17, D Shoda18, V Seyfert-Margolis14, EV Sigal19, J Sobotka20, D Tan12, TF Unger18 and G Hirsch2

Traditional drug licensing approaches are based on binary decisions. At the moment of licensing, an experimental therapy is presumptively transformed into a fully vatted, safe, efficacious therapy. By contrast, adaptive licensing (AL) approaches are based on stepwise learning under conditions of acknowledged uncertainty, with iterative phases of data gathering and regulatory evaluation. This approach allows approval to align more closely with patient needs for timely access to new technologies and for data to inform medical decisions. The concept of AL embraces a range of perspectives. Some see AL as an evolutionary step, extending elements that are now in place. Others envision a transformative framework that may require legislative action before implementation. This article summarizes recent AL proposals: discusses how proposals might be translated into practice, with illustrations in different therapeutic areas; and identifies unresolved issues to inform decisions on the design and implementation of AL.

Clinical Pharmacology & Therapeutics (2012); 91 3, 426-437. doi:10.1038/clpt.2011.345

March 2014: EMA Pilot Program

European Medicines Agency launches adaptive licensing pilot project

Improving timely access for patients to new medicines: pilot explores adaptive licensing approach with real medicines in development

The European Medicines Agency (EMA) is inviting companies to participate in its adaptive licensing pilot project. Companies who are interested in participating in the pilot are requested to submit ongoing medicine development programmes for consideration as prospective pilot cases.

A framework to guide discussions of individual pilot studies has been published.

The adaptive licensing approach, sometimes called staggered approval or progressive licensing, is part of the Agency’s efforts to improve timely access for patients to new medicines. It is a prospectively planned process, starting with the early authorisation of a medicine in a restricted patient population, followed by iterative phases of evidence gathering and adaptations of the marketing authorisation to expand access to the medicine to broader patient populations.
Adaptive regulation is one key enabler to serve our patients and society in the future - A joint effort is needed to advance

Thank you!

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