FDA - EMEA Interaction
Implications for the Pharmaceutical Industry

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Competitive global environment and high development costs demand for one efficient global drug development program appropriately proving safety and efficacy and providing access to all major markets.
Information-Sharing Agreement
FDA/EU signed by FDA, EMEA, and EC September 2003

- EU-FDA bilateral meetings since 1989
- PhWG/FDA monthly videoconferences on Pharmaco-vigilance
- Now strengthening communication in step wise approach to include - orphan drug designation
  - inspection reports
  - marketing approvals
  - post-authorisation surveillance information
  - parallel scientific advice
EMEA perspective

• Confidentiality of non-public information will be protected
• Industry benefit: opportunity for parallel Scientific Advice
  [EMEA Press release Sep 2003]
• More focus on global development is required, but very resource intensive  [T.Lönngren at DIA March 2004]
• Parallel SA only when the company is volunteering
  [D.Brasseur at DIA March 2004]
• Company may potentially be involved immediately after conference  [M.Toivonen at DIA March 2004]
FDA perspective

- Share important information about
  - pending approvals
  - post marketing surveillance
  - enforcement actions

- To build understanding and mutual confidence [FDA Report 2003]
- Joint Advice can occur in a number of ways, including
  ...a videoconference...with company representatives [M Lumpkin, RAJ Nov 2003]

- Joint policy development [S.Hirschfeld DIA, March 2004]
Parallel Scientific Advice (pSA)

- First experience
- Background: Current advice procedures EMEA/FDA
- Benefits of pSA from industry perspective
- Risks of pSA from industry perspective
- When should Industry use pSA
- What industry would really need
First parallel EMEA-FDA Scientific Advice procedure (pSA)  
September 2003

• For orphan drug at request of the sponsor  
• During Protocol Assistance (PA) after oral EMEA hearing  
• Prior to EoP 2 meeting at FDA  
• Videoconference of EMEA and FDA assessors  
• Chaired by M.Toivonen, observer T.Lönngren, M. Lumpkin  
• On scientific issues on the proposed development plan  
• FDA / CPMP continue to adopt advice independently
pSA experience from EMEA perspective

• High expectations/interest from sponsors
• EMEA already before requested FDA advice from sponsor
• Each agency remains responsible for its own advice [M. Papaluca Amati, at CMR Sept 2003]

• Parallel SA provides arena for agency discussion but outcome is not binding for any side [T. Lönnegren at DIA March 2004]
• Two further requests for parallel SA received
• Points for discussion on preclinical and clinical issues [M. Toivonen at DIA March 2004]
EMEA Scientific Advice - survey 2003

Jan - Sep 2003
n=41 questionnaires, 36 SA and follow up, 6 PA

58 % Clinical questions (thereof 56 % Phase III related)
26 % Preclinical questions

12 % found advice very different from the one received from other authorities

19% had to devise a completely different development plan after the advice

[Prof M Toivonen, DIA meeting March 2004]
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Impact of EMEA Scientific Advice on approval chances

In 2003, up to 45% of applicants for Marketing Authorisations received prior Scientific Advice or Protocol Assistance

Chances of favourable outcome at the time of the opinion of the CPMP show positive correlation with prior SA / PA

[9th Annual report EMEA activities 2003]
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FDA Scientific Advice during drug development

[Innovation or Stagnation, FDA Report March 2004]
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2003 EMEA SA, PA and FDA SA meetings, SPA requests

![Graph showing the number of meetings for EMEA SA, EMEA PA, FDA SA, and FDA SPA. The graph indicates a significant increase in SPA requests compared to other categories.](graph_image)
Industry perspective - Benefits pSA

• Allows for discussion and maximal information exchange on scientific issues

• Fills gaps if no guideline or precedent is available (see also announced shared guideline development)

• Strengthens Regulators guidance / impact during development

• Avoid unnecessary study replication in the two regions if agreement can be reached on an appropriate level - one efficient global development plan
Scientific Advice timelines FDA/EMEA

- **Meeting**
- **Final Advice**

### Timelines:
- **Notification**
- **Assessment period**

**FDA SA**
- 0 months
- Assessment period
- Final Advice

**FDA SPA**
- 0 months
- Assessment period
- Final Advice

**EMEA SA/PA**
- 0 months
- Assessment period
- Final Advice

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EMEA outcome for **FDA positive** applications (n=139)

- EMEA Negative 20%
- EMEA Positive 80%

35 products for which CPMP voted negative were approved by FDA

[E. Abadie, CMR Workshop Sept. 15/16 2003, Washington]

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Industry perspective - Risks of pSA

• Missing transparency
  - procedure so far not formally described
  - industry not allowed to participate
  - there will be no joint outcome document

• Not really joint but parallel, outcome may differ

• Risk for higher hurdles (group dynamics, differences in therapeutic environment)

• Prolongs overall timelines for authority advice
When should Industry use pSA?

- For issues that can be solved on scientific level independent of therapeutic environment
- For conflicting EMEA/FDA advices that are major obstacles to further development
- If access to all markets by full program not speed to market is driver of development
- If CPMP and FDA guidelines deviate considerably
- To harmonise comparator treatment
- To benefit from special expertise of one authority
What Industry would really need

Transparency !
- Inform on preliminary advice to allow for pSA
- Industry participation in meetings

Flexibility !
- If deviations in separate advice, follow up pSA
- Shorten SA procedure
- Compromises supporting globalisation

Simplify !
- Effective and simple meeting structures for (too many) stakeholders
FDA / EMEA co-operation - Good News

- Possibility for interaction facilitates global development
- EMEA, national EU authorities interested in FDA position

...Not yet so Good News

- Conflict resolution?
- Sponsor involvement
- Increased FDA/EMEA information share w/o procedures
  - risk of preliminary / incomplete information
- Procedures/Guidelines to be developed for all areas
- FDA not yet asking for CPMP position
- What is the impact on ICH?

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BACK UP
### Approval procedure in EU and US

#### Priority NDA
- Assessment period: ~180 months
- Company Response time: ~60 months

#### Standard NDA
- Assessment period: ~300 months
- Company Response time: ~60 months

#### Centralised MAA
- Assessment period: ~120 months
- Agency letter: ~52 months
- Potential meeting dates: ~30 months

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Priority NDAs
Actions, filings*, approval percentages

Calendar year
* A filing in one year may lead to several actions or an approval in subsequent years.

Number

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Percent

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Figure 2: 10-Year Trends in Major Drug and Biological Product Submissions to FDA

- Total NMEs Rec’d by FDA
- Original BLAs

Innovation or Stagnation, FDA March 2004

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Parallel Scientific Advice - Timelines

• Meeting co-ordination major challenge for project managers, inform well in advance

• Parallel approach needs exact timing

• Feedback in writing is no option in this case

• Delay by 2 m expected compared to conventional procedure
Figure 3: Investment Escalation per Successful Compound

Investment required for one successful drug launch (discovery through launch)

$1.7B
Launch

$1.1B
Preclinical

Critical Path

Discovery

Phase I

Phase II

Phase III/File

Critical Path

Discovery

Phase I

Phase II

Phase III/File


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Can consensus be reached?

35 products for which CPMP voted negative were approved by FDA

20 of them FDA approved even without Advisory Committee meeting

Submissions were not more than 2 years apart from each other

[E. Abadie, CMR Workshop Sept. 15/16 2003, Washington]
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