EMEA/CHMP Think-Tank group on Innovation

To form a critical view on the current and future scientific development of medicinal products and related regulatory standards in Europe:

- To identify bottlenecks in the development of medicinal products
- To identify possible redundant or irrelevant regulatory requirements
- To discuss the application of new methods and procedures in the development and regulation of medicinal products
- To support European Commission in Innovative Medicines Initiative
- To facilitate discussions between CHMP, academia and industry on innovative approaches for the development of medicinal products

EMEA-CHMP Think-Tank group on Innovation

• Meetings with 14 pharmaceutical companies 11/2005-2006
• Meetings with academic groups 4Q/2006:
  - EASD (European Association for the Study of Diabetes)
  - EFNS (European Federation of Neurological Societies)
  - EORTC (European Organisation for Research and Treatment of Cancer)
  - ESCMID (European Society for Clinical Microbiology and Infectious Diseases)
• Final Report: March 2007

EMEA-CHMP Think-Tank group on Innovation

1. Communication and interaction with regulators during the lifecycle of the products
2. Global harmonisation
3. Emerging science for clinical development and regulatory approval
   3.a Translational development, clinical methodology
   3.b Advanced Therapies
4. Pharmacovigilance
5. Guidelines
6. Antimicrobials

EMEA-CHMP Think-Tank group on Innovation

• Areas for improvement in the EMEA/CHMP operations
  - Communication during the lifecycle of the product
  - Guidelines
• Scientific topics
  - Biomarkers
  - Statistical methods and clinical study designs
  - Faster access tools
  - Risk Management Plans
• Areas for the attention of the EC and NCAs in the EU Network
  - Guidelines for Clinical trials
  - Global aspects
  - Interaction between Industry and Academia
  - Advanced Therapies
• Special public health topic: Antimicrobial resistance

Participants of the EMEA-CHMP Think-Tank group

- Daniel Brasseur, Chair
- Gonzalo Calvo Rojas
- Bruno Flamion, Vice Chair
- Bengt Danielsson
- Robert Hemmings
- Pekka Kurki
- Ingemar Persson
- Patrick Salmon
- Cristina Sampaio
- Bo Aronsson
- Emer Cooke
- Xavier Kurz
- Patrick Le Courtois
- Xavier Luria
- Ouli Maki-Ikola, Project Manager
- John Purves
- Agnes Saint-Raymond
- Spiros Vamvakas

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Final Report: March 2007
Think-tank’s: recommendations for action

Which approach has been taken for implementation

1. Interactions with stakeholders: in depth and well prepared discussion meetings 2005-2006 ➔ «signals» for action undertaken immediately by the EMEA
2. Think-tank Report published March 2007
3. Plan for implementation agreed by the CHMP Dec 07
4. EMEA Executive launches an EMEA-wide process improvement project (ongoing)
5. CHMP work programme 2008-2010

Think-tank’s: recommendations for action

Which approach has been followed for implementation

Actions undertaken within the frame of the EMEA improvement exercise for operations in the area of Human medicines

- Improved procedures
  - OMP: better use of resources
  - SA: implementation pre-submission, shorter timelines and extended involvement of expertise via IT methods
  - Pharmacovigilance referrals: streamline of procedures and better information to the public
  - Plasma master files: better information
  - Pharmacovigilance: improvement in signal detection
- Improved CHMP and working parties meetings management

Areas for action agreed with the CHMP (1)

1. Areas for action with general impact
   IMI, interaction with networks, modernisation of working and communication methods
2. Communication and interaction during the lifecycle of the products
   Early dialogue on innovation, scientific advice, gap between SA and MAA
3. Global harmonisation
   ICH, Bilateral arrangements

Areas for action agreed by the CHMP (2)

4. Emerging science for clinical development and regulatory approval
   - Support to early clinical development, translational medicine
   - Innovative R&D methods including biomarkers, new imaging techniques, modelling and simulation, new statistical approaches
   - Faster access tools: conditional approval and accelerated review
   - Advanced therapies
5. Pharmacovigilance
6. Guidelines
7. Antimicrobials

1. Innovative Medicines Initiative

EMEA Policy on the participation in Innovative Medicines Initiative (IMI) – research projects published May 2008)
In response to this paper 10 consortia requested EMEA to participate

Advisory body for decisions established (SMO)

EMEA partner of a consortium
EMEA leading an applicant consortium to address the call for “Strengthening the monitoring of Benefit-Risk”

Making partnership to happen and establishing the grounds for transparent and fair future involvement: requests for participation to consortia have now their pathway.

1. Interaction with networks

- ENCePP network: phase 1 of the project completed. Five ENCePP working groups active. Representatives of learned societies members of the ENCePP Advisory Board
- Paediatric network: implementation strategy published Jan 08; to foster high quality ethical research on medicinal products to be used in children, strengthening scientific, technical and/or administrative competences in the performance of paediatric clinical trials ➔ Coordination group to start in 2009
- New process for Learned societies and stakeholders active consultation on EMEA scientific work: database and procedures being established (MIS) ➔ 2009
- Activities of the HCP and PO working group: reinforced contribution to EMEA activities in 2009
1. Modernisation of working and communication methods

- WEB Sharing and video/Tc conferencing implemented in CHMP, SAWP and increasingly in other working parties to optimise availability of expertise
- Training sessions on key areas reinforced by the use of IT media (e.g. Paediatrics and ATPs)
- Paperless working method (MMD) successfully implemented in CHMP and extending to working parties (e.g. SAWP, BWP)
- eCTD submission of applications implementation plan (ongoing)
- EMEA scientific publication policy and publication review group established May 08

2. Communication in the lifecycle of the products

Scientific advice: further improvements

- Peer review by CHMP: introduced mid 2007 (positive impact in 30% of the cases). To be consolidated in 2009
- End-of-phase 2 advice: "guaranteed" discussion meeting with SAWP in case of divergent views
- EMEA/FDA SA: available but no requests received from sponsors
- New procedures for minor SA follow-up/clarifications: to be formalised in 2009

3. Global Harmonisation

Bilateral arrangements with FDA

- Collaboration with FDA ongoing on established clusters (e.g. paediatrics, OMPs, oncology, pandemic flu, pharmacogenomics, qualification of biomarkers)
- New initiatives being undertaken in the area of ATPs
- Initial steps taken in the area of nanomedicines (for further action in 2009)
- Bilateral EC-EMEA/FDA will define the new clusters

New bilateral confidentiality arrangements

- Bilateral arrangements with Japan and Canada in the implementation planning phase
- Exchange of officials and visits with FDA and PMDA MHLW
- Identification of a new function in Directorate and Executive to support for international liaison
3. Global Harmonisation

Maintain the focus on ICH activities

- ICH Q8 Annex Pharmaceutical Development – step 3 comments by May 08
- ICH Q9 Quality Risk Management: planning EU implementation
- ICH Q10 Pharmaceutical Quality System: planning EU implementation
- ICH S2 genotoxicity guideline - rev. comments by May 08
- ICH S6 - Preclinical Safety Evaluation of Biotechnology-Derived Products
- ICH M3 (Non-Clinical Safety Studies for the Conduct of Human Clinical Trials for Pharmaceuticals) - rev. 2 comments by Oct 08
- ICH E2F Development safety update reports (comments by Dec 08)
- E7 studies in elderly: concept paper for revision adopted by SC
- ICH E16: PG biomarker qualification dossier structure and data format
- Gene Therapy: oncolytic viruses and shedding studies reflection papers

4. Science in clinical development and regulatory approval

Translational medicine

- Biomarkers
  - Global collaboration: ongoing with FDA, planned in 2009 with PMDA and Health Canada
  - Participation in consortia (IMI, C-Path): EMEA/CHMP actively involved in C-Path PSTC consortium
  - Workshops:
  1st held in 2005 and 2nd in 2006
  2. Pilot BM qualification process in 2007
  3. Formal BM qualification process implemented in 2008

Clinical methodology

- Statistical aspects /new study designs
  - Flexible design and Bayesian approach discussed in the EWP
  - Reflection Paper on Methodological Issues in Confirmatory Clinical Trials planned with an adaptive design
  - CHMP work programme project: establishing in 2008 a group with statistical expertise:
    - Support a consistent science-based approach
    - Workshops
    - Training
    - Specialised network

Faster access tools

- Conditional approval and RMP: implemented in scientific advice and final opinions
- Accelerated review: CHMP work programme project 2008-2010:
  - Analysis of the experience
  - Identify obstacles
  - Propose measures to improve success of the provisions

EMEA promote dialogue on innovative R&D

Workshops on scientific priority areas identified:

- 2006: Design Space, Slowing the Progression of Neurodegenerative Diseases, Biomarkers
- 2007: Workshops on requirements for first-in-man clinical trials for potential high-risk medicinal products, Joint with EC workshop on clinical trials, Immunogenicity Assessment of Therapeutic Proteins, Cell based medicines, Gene therapy vectors shedding, adaptive design in confirmatory trials
- 2008: Neurodegenerative Diseases - Focus on Dementia, Modelling in paediatric medicines, Brain Diseases in the Elderly, Clinical Outcome Measures and endpoints for efficacy assessment in spinal muscular atrophy, Integrating PG BM into Drug Development: PK as a working example
- 2009: New statistical methods

Participation in consortia (IMI, C-Path, E-Most, C-Path, EMEA promote dialogue on innovative R&D

Think-tank’s: recommendations for action
4. Science in clinical development and regulatory approval

Think-tank’s: recommendations for action

Advanced Therapies

New Guidelines/ Reflection papers/ Question and Answer-documents
Contribution to the EC implementation plans
Classification and certification of quality and non-clinical data for SMEs
Rolling scientific evaluation
CHMP and CAT

5. Pharmacovigilance

Guideline on safety and efficacy follow-up/risk management of ATMPs:
Facilitate access to Eudravigilance data/ signal detection tools:
- Access on communication signals: reflection stage
European network of centres for pharmacoepidemiology and pharmacovigilance: Advisory Committee and 5 working groups established.
Next meeting Oct.08
Update risk management system-guideline: Action 2009
Workshop on effectiveness of RMPs: Action 2009

6. Guidelines

Consultation of experts and stakeholders
Implemented via public workshops on key principles at very early stage and/or prior finalisation to address major comments
- Priorities for guideline development on the basis of the needs of product development to be established in consultation with stakeholders
- Reconsider the balance between general guidance (retrospective) and individual (prospective) advice
Issues under consideration in the dedicated project of the CHMP working programme 2008-2010

7. Antimicrobials

Gap analysis on current medical needs for antimicrobials, priority list of pathogens
Joint CHMP/PDCO WG with ECDC + Collaboration established with Duke University and REACT and with EBGMID (European Society)
- agreement on pathogens priorities for drug development
- establishment of search criteria and searches run on databases to identify products in development (Phase I to III plus pre-registration)
- rating agreed and being assigned to products that cover any of the priority pathogens
Tailor-made requirements to encourage development of new antimicrobials (4th Q 2009)
Initiatives for incentives for developing old antimicrobials or niche product (4th Q 2009)
CONCLUSIONS

- Implementation of action in all areas identified by the Think Tank has major impact on EMEA operations and resources
- Work in progress or clearly planned for most TT recommendations
- Ongoing efforts to integrate synergies among all stakeholders involved
- Implementation to take into account experience, evolution of the needs and the changing pharmaceutical environment (e.g. new legal provisions)

Thanks for your attention!
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BACK UP SLIDES

1. Communication and interaction with regulators
   - Briefing meetings to be further developed
   - Faster scientific advice
   - SA peer review
   - Pre-submission meetings for MAA with extended scientific discussions

2. Global harmonisation
   - Routine discussions with other regulators (FDA) on biomarkers, new statistical approaches, risk management plans, advanced therapies, parallel SA

3. Emerging science
   - 3a Translational development, clinical methodology
     - Involvement in the US Critical path Initiative and support to the European IMI, workshops and training, reflection papers, early involvement in biomarker development and acceptance, further resources on statistical methods, links with European and international statisticians, EWP subgroup on adaptive designs and other statistical aspects.
   - 3b Advanced Therapies
     - New Guidelines/ Reflection papers/ Question and Answer documents, contribution to the EC implementation plans, informal dialogue opportunities, rolling scientific evaluation and certification of quality and non-clinical data for SMEs

4. Pharmacovigilance
   - Update risk management system-guideline
   - Encourage SA on risk management plans
   - Analyse and develop principles for acceptable standards in risk minimization activities
   - Workshop on effectiveness of RMPs
   - Facilitate access to EudraVigilance data/ signal detection tools, Establish European network of centres for pharmacoepidemiology and pharmacovigilance

5. Guidelines
   - New, quicker Question and Answer-documents
   - More Reflection Papers
   - More focussed guidance
   - Specific assessor networks
   - Prioritisation + early consultation of experts and stakeholders, guideline on drug diagnostic co-development
6. Antimicrobials
   Gap analysis on current medical needs for antimicrobials priority list of pathogens: joint CHMP/PDCO WG with ECDC to define and supervise its progress
   Tailor-made requirements to encourage development of new antimicrobials