Implementierung des Review aus Sicht der EMEA

7. DGRA - Jahreskongress, Bonn 9. Juni 2005

Sabine Haubenreisser, Dr. phil. nat. - EMEA

Agenda

- Integration of the New Member States
- Consequences on the activities of the CHMP and the EMEA
- Achievements so far

Revised Legislation

- Enlargement to 25 Member States 1 May 2004
- Title IV of Regulation (EC) No 726/2004 implemented on 20 May 2004
- Rest of Regulation (EC) No 726/2004 implemented 20 November 2005

New Team

Review 2001	Enlargement
2 members / MS →	30 + 2 + 2 →
1 member + 1 alternate	25 + 2 + 5
Plus up to 5 co-opted members	Plus alternates

Attendance Records (Sep 04 – May 05)

	Members	Alternates	Experts
Sept '04	30/0	14	29
Oct '04	28/3	15	19
Nov '04	27/3	10	33
Dec '04	31/1	9	24
Jan '05	29/1	11	25
Feb '05	29/3	15	25
March '05	27/3	12	28
Apr '05	27/4	12	51
May '05	30/2	11	26

Co-opted members – Complementary Expertise

- CHMP moved quickly to take up option
- Complement expertise of the CHMP
- Chosen specific scientific competence
- Term CHMP/renewable/no alternates
- Rapporteur/associate national delegation

Co-opted members – Complementary Expertise

- Manfred Haase - Blood Products
- Pekka Kurki - Biotechnology
- Ingemar Persson - Pharmacovigilance
- Jean-Louis Robert - Quality
- Frances Rotblat - Pharmacovigilance

Industry concerns

- Committee dynamics/voting process
- Applicability of scientific advice
- Appointment of Rapporteurs
- “Predictability of Outcome”

Preparatory Steps

- New Member States Observers as of 1 April 2003
  - Supply of MAA components and assessment reports as of 4 Q/03
- Training sessions – June to September 2004
  - Good attendance
  - Old and new mixed

Preparatory Steps

- Conflicts of Interest/Confidentiality process
  - DoIs published on website
  - Constant "challenge" for public confidence
- Roles and responsibilities of
  - CHMP Members and Rapporteurs/Co-Rapporteurs
  - Experts
  - EMEA Secretariat

Concern about voting process not substantiated by experience

- Simplified procedures = many years
  = high % acceptance
- PERF process/observerships/exchange information = confidence building trust
- No 'bloc' approach = variability as per CHMP
- New Roles & Responsibility guidance focuses on contact via Rapporteurs vs direct to Members

Practical impact of the enlargement

- Members directed to work for consensus whenever possible
  - Chair/Vice Chair continuity
  - No abstentions (except in case of conflict of interest)
- Language regime EN
  - not to be underestimated as facilitating the workload capacity of CHMP

Rapporteurships

- Ongoing evaluation/post-authorisation procedures
  - "Turnover" rate CHMP members/alternate
  - Rapporteurs have remained under nominating national delegation
  - "Skewed" distribution Rapporteurships
  - Appointment of Rapporteur
    - Objective criteria
    - Best available expertise
    - Relevant scientific area
    - Peer Review System may offer more opportunity increased involvement

Alternates

- Shall represent and vote in absence of a member
- Can fulfil the role of the Rapporteur – "at any time"
  - Reimbursed attendance at meeting where products are discussed
  - Attendance level ranges 11 – 18/meeting
  - Substitution level 0 – 4/meeting/part meeting

New member extended role

- Working Parties
  - Mix "1/national delegation" and "as needed" scientific competence
  - Nominated and agreed by CHMP
  - Chairs tend to be from "old" EU

Scientific advisory groups

- Previous TAGs became SAGs:
  - Anti-infectives, Oncology, Diagnostic
- Rules of procedure adopted
  - External experts proposed by CHMP Members or EMEA
  - European Expert List
  - Core group + specialised experts as needed
  - Role
- General and specific mandates adopted
- Creation of New SAGs in 2005:
  - Endocrinology/ Diabetes, HIV/ Viral diseases, CNS/ Psychiatry and Cardiology

Scientific advice working party

- Mandate adopted, composition agreed
- New Procedure proposed to CHMP in April 2004
- Final proposal to be discussed with Heads of Agencies in July 2005

Further Preparation for Implementation

- EMEA internal task force: EMEA sponsors and team
- CEITAF (CHMP/EMEA implementation task force) involvement of CHMP members
- Implemented in January 2005 – started in February '05
- Task force meets in margin of CHMP meetings
- EMEA reports on achievements in the monthly CHMP report

Task Force at EMEA

- EMEA Meeting with Heads of Agencies representatives 4 April 2005

- Consultation with
  - Member States through MRFG and Commission consultation (NTA, Emacolex, Pharmaceutical Committee)

- Agreement from European Commission (DG Enterprise) on interpretation

Implementation Task Force

Planned timeframe for Implementation of Regulation 726/2004 at EMEA Level

November 2004

EMEA task force

January 2005

Preparatory Work & Drafts

February 2005

CHMP Contribution

May 2005

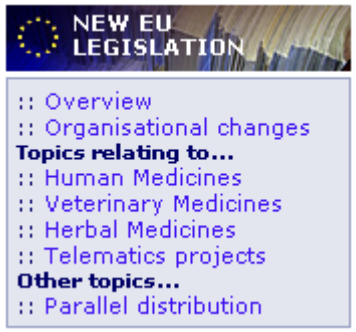
June/July 2005

External Consultation

July /September 2005

Finalisation

October 2005



The main topics in the Pre-authorisation phase (1/6)

- Opinion on Compassionate Use (GL)
  - Product eligible for centralised procedure
  - During clinical trials, or
  - At time of marketing authorisation application
  - Major Public Health Interest

The main topics in the Pre-authorisation phase (2/6)

- Mandatory scope (GL)
  - Treatment of cancer, diabetes, AIDS, and neuro-degenerative diseases
  - Orphan medicinal products
  - Prevention, diagnosis, staging/ monitoring, not included
  - Treatment targeted as palliation or relief of associated complications/ conditions not included
  - Treatment of adverse reactions caused by other treatments of the disease not included

The main topics in the Pre-authorisation phase (3/6)

- Optional scope (Reflection paper)
  - Not authorised
  - Innovation
  - Interest of patients

The main topics in the Pre-authorisation phase (4/6)

- Choice of Rapporteurs (GL)
  - Criteria for best expertise
- Accelerated Assessment (GL)
  - Eligibility criteria: Major interest for public health, e.g. innovation
  - Timelines (80d, 150d), procedure

The main topics in the Pre-authorisation phase (5/6)

- Conditional Marketing Authorisation (CR, GL)
  - Draft Commission Regulation (CR)
  - Eligibility: Public Health Interest, fulfil unmet medical need (Orphan Drugs, emergency/ threats, chronic, serious, life-threatening conditions)
  - Demonstration of a positive benefit/risk balance, pending completion of further studies
  - One year renewable

- Exceptional Circumstances (GL)
  - Criteria to be fulfilled
  - Specific Obligations
  - Benefit/Risk Assessment once a year

The main topics in the Pre-authorisation phase (6/6)

- Re-examination of opinions (GL)
  - Ex-appeal procedure
- Publication of withdrawals (Reflection paper)
- Summary of EPAR for the public (Reflection Paper and Template)

The main topics in the Post-authorisation phase (1/4)

- Data protection issues
  - 8 years, then access for generics, but 10 years of market protection
  - 1 year additional for new indication of significant clinical benefit vs existing therapies (GL)
- Well-established substance (GL)
  - 1 year covers only data related to the new indication

The main topics in the Post-authorisation phase (2/4)

- Renewals
- Actual Marketing and Cessation of Placing on the Marketing
- Sunset Clause

The main topics in the Post-authorisation phase (3/4)

- Risk management (GL)
  - Link with ICH E2E
- Compliance with pharmacovigilance (GL)
  - Supervision and advice
- Urgent provisional measures
- PSUR's cycle

The main topics in the Post-authorisation phase (4/4)

- Pharmacovigilance communication
- Transmission of infectious agent via a medicinal product
- Eudravigilance

Conclusion

- Implementation of the New Legislation is EMEA priority for 2005
- Important part achieved through set up of New Committees, Working Parties and Groups
- Neither dysfunction nor delays in management of procedures
- Dedicated page for review implementation issues on EMEA website: www.emea.eu.int

EMEA Implementation of the New EU Pharmaceutical Legislation

Overview
- The new legislation
Organisational changes
Topics relating to human medicines
Topics relating to veterinary medicines
Topics relating to herbal medicines for human use
Telematics projects
Other topics
- Parallel distribution

Publication and consultation of EMEA guidance documents implementing the new pharmaceutical legislation

The table below is intended to inform Interested Parties in a timely manner about development at the EMEA, as part of the implementation of the new pharmaceutical legislation, of procedural or clarification documents/guidelines in relation to human medicinal products. External consultation is expected to be held for each of the documents/guidelines listed. Unless otherwise specified, the **consultation period for each document/guideline will be four weeks**.

Please note that the current list of documents is not exhaustive and that titles of draft documents are for indication only, pending discussion within the CHMP during its specific Implementation Task Force (CEITAF) meetings. The table will be updated to reflect changes as and when they occur.

Relevance to Medicinal Products for Human Use

☐ Draft ☐ Adopted ☐ Anticipated

Updated on 03/06/2005

Topic	Title of document	Consultation		Send feedback to:	Additional information
		Start	End		
CHMP opinion in collaboration with the WHO	Guideline on procedural aspects regarding a CHMP scientific opinion in the context of cooperation with the World Health Organization (WHO) for the evaluation of medicinal products intended exclusively for markets outside the Community (EMEA/CHMP/5579/04)	N/A	N/A	N/A	FINAL GUIDELINE ADOPTED FOR IMPLEMENTATION
Scope mandatory indications	Draft Guideline on therapeutic areas within the mandatory scope of the centralised procedure for the evaluation for marketing authorisation applications with reference to Article 3 and the Annex of Regulation (EC) No 726/2004 (EMEA/180921/2005)	03/06/05	08/07/05	Denisa.DeChiara@emea.eu.int	
Product information	Updated human Product Information templates – Human medicinal products (EMEA/100388/2005)	23/03/05	20/05/05	qrd@emea.eu.int	
Principles of good manufacturing practice for active substances used as starting materials	Medicinal Products for Human and Veterinary Use: Good Manufacturing Practice - Basic Requirements Part II: The Principles of Good Manufacturing Practice for Active Substances used as Starting Materials (EMEA/INS/GMP/15202/2005)	08/03/05	04/04/05	sabine.atzor@cec.eu.int and gmp@emea.eu.int	The Commission has published this document for consultation on its website at: http://pharmacos.eudra.org/F2/pharmacos/new.htm