Managing regulatory uncertainty in rapidly emerging areas: pharmacogenetics

European Medicines Agency
Perspectives and strategies

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Presentation outline

General considerations

EMEA strategy

(http://www.emea.eu.int/htms/general/direct/roadmap/roadmapintro.htm)

Conclusions

Why venturing in uncertainties ?

1. **Large majority (>80%) of compounds entering clinical trials fails because of toxicity or unsatisfactory efficacy. (50% phase III fail for safety/efficacy reasons)**
   - **Risk of pipeline draught**
   - **~30% failure of MAAs in the centralised procedure**
2. **Significant labelling restriction at the time of approval and within the first two years after launch**
3. **Two or more valuable medicines per year withdrawn because of serious ADRs (1991 and 2004)**
4. **Current mortality and morbidity due to ADRs or insufficient efficacy**

Impact on individual patients,

public health, industry

PG potential

- Greater understanding of patho-physiology and subtypes of diseases
- More efficient science-based drug design, prediction of efficacy and management of toxicity in drug development
  - **Better target identification and improved selection of candidate compounds**
  - **Higher POS in the pipeline**
- More appropriate drug and dose selection in a better defined population or individuals
  - **Improved benefit/risks balance**
  - **Less treatment failures and withdrawals**
- More vigorous and productive industry

Regulators' responsibilities

Protecting public health by assessing benefit/risk balance and risk management of drugs

Promoting strategies and technologies for optimal development of innovative medicines

Contributing to the societal debate providing independent information

for the attainment of both industrial and public health sector goals

Managing regulatory uncertainty in rapidly emerging areas

- Ensure science-based regulatory environment and strengthen the regulatory processes
- Be proactive in facts finding and encourage innovation to come forwards in the Regulatory arena: create new structures and processes to adjust for complexity
- Discuss issues and solutions with stakeholders so to anticipate impact on current practices and policies
- Support international efforts to develop harmonised global understanding and standards

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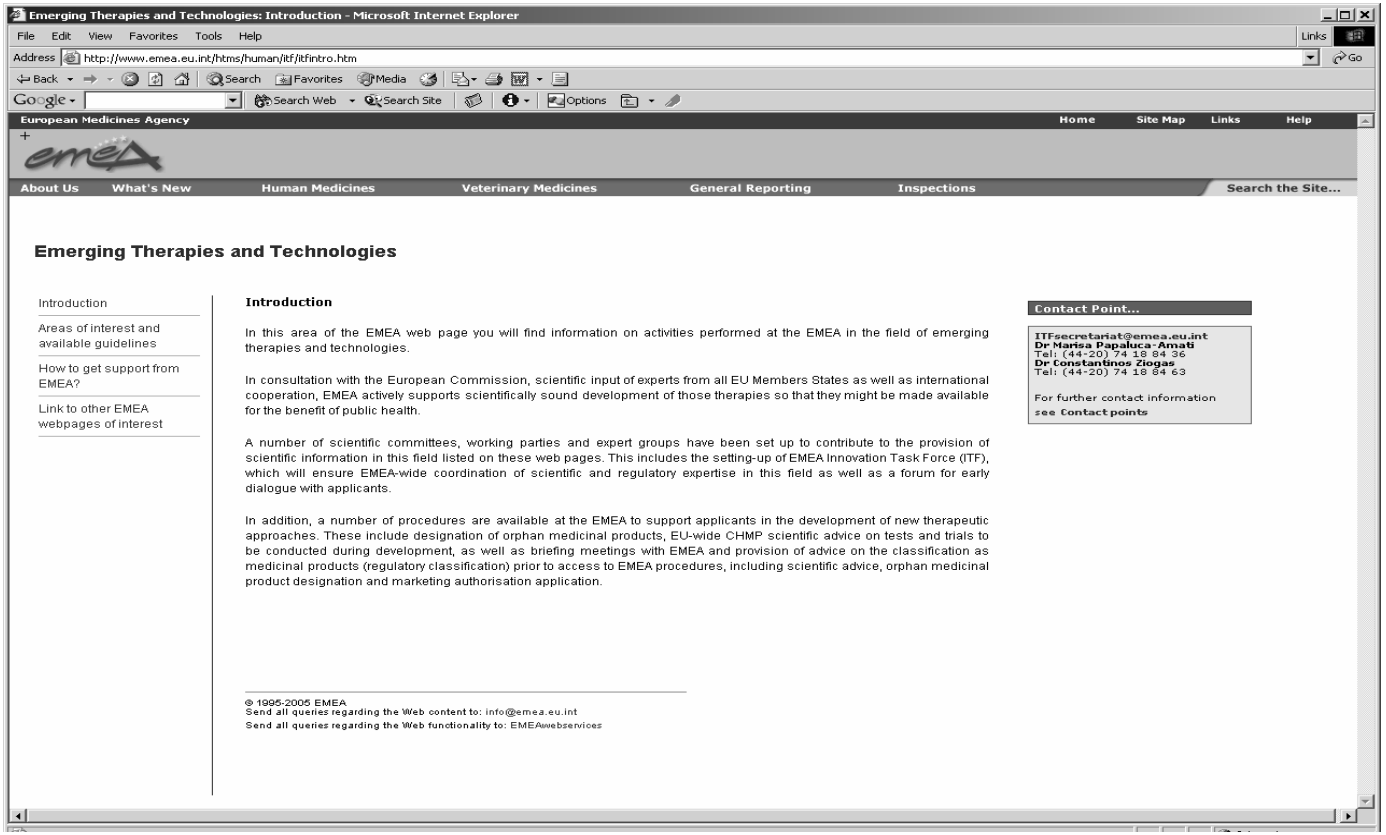
Managing regulatory uncertainty in rapidly emerging areas Structural adjustments

EMEA Innovation Task Force (ITF)



CHMP PG Working Party

http://www.emea.eu.int/pdfs/human/pharmacogenetics/10159204en.pdf

- **Share experience on issues arising from the integration of pharmacogenetics in drug development, assessment and information**
- **Prepare, review and update guidelines**
- **Support dossier evaluation and contribute to scientific advice**
- **Advise on Pharmacogenetics related issues the European Commission**
- **Liaise with interested parties**
- **Support European and international cooperation**

PG Working Party: new structure

Chairperson E. Abadie
Vice-Chairperson: B. Flamion

50% academia scientists

50% regulatory scientists

+ “area” specialists and industry’s scientists invited for PG briefing

PG briefing: new process

What is a PG briefing meeting?

A new way of submitting preliminary data

A new informal dialogue among Regulators, Academia and Industry scientists on emerging science

A new way to reduce uncertainties for further research, development and decision making

A tool for raising awareness and training

A good operational model for tackling innovation

PG briefing: a new process

What a PG briefing meeting IS NOT

- A Scientific Advice pre-submission meeting
- A CHMP scientific advice on how to implement PG in the development program
- A preliminary MAA data assessment

PGWP activities

Released documents:

- **Terminology in PG**
- **Draft Guideline on briefing meetings: format and content**
- **Concept paper on biobank issues relevant to pharmacogenetics**

Upcoming public documents

- **Revised paper in lay language "Understanding the terminology used in pharmacogenetics"**
- **Concept paper on impact of PG on PK studies**
- **Revised PGWP Workprogramme 2006 +…..**

PGWP activities

Workshop 2003 on PG in clinical development (DIA plat.)
Workshop 2004: do we need further regulation
Seminar with Industry Dec 2005: biobanks issues

Eleven briefing sessions + 3 scheduled Dec 05
2 PG platforms sponsors + 12 Drug sponsors

Therapeutic areas

- Diabetes, Obesity
- Depression
- Rheumatoid arthritis, transplantation, asthma
- Cancer
- Hypertension, Myocardial Infarction

Examples of scenarios discussed at PG briefing meetings

- Genomic expression signature as a biomarker bridging proof-of-concept from animal model to man

- Data from pre-collected samples. Potential regulatory value in conducting retrospective PG biomarkers analyses and impact on existing and new drugs

- Genomic markers in prospective studies. Methodological options.

- Determination of the PG clinical utility (clinical magnitude of the differential response, benefit in clinical outcomes using the PG test) and labelling implications

Managing regulatory uncertainty in rapidly emerging areas

Support to European and international harmonisation

Support to european and international harmonisation

- Contribution to relevant EU initiatives
- Contribution to international debate on PG (e.g.DIA workshops, CIOMS Expert group, OECD)
- Implementation of confidentiality arrangements with FDA
- ICH

Challenges to PG potential development

- Samples collections and data pooling
- PG Biomarker “validation” data requirements
- Population genetic ancestry impact
- Co-ordination of submission of drug and test data pre and post approval
- Clinical validity/utility
- Impact on the label and on risk management and minimization (including educational programmes)

Challenges for PG development: biobanks

- **Concept paper released March 2005**
  - **maintenance in biobanks of identifiable samples for pharmacogenetics use, the duration of their availability versus the handling of anonymous or anonymized samples**
  - **scientific needs and objectives of the regulatory oversight**
  - **issues relevant to the scientific validity of pharmacogenetics studies**

Challenges in EU for PGx products: biobanks

- Points to consider in defining the procedures for collecting, storing, handling/curing and analysing samples and relevant data for pharmacogenetics purposes

- Implications of removing from samples and data identifying information in pre and post authorization assessment of medicinal products

- Systems of quality assurance and quality control

Issues discussed on PG-driven co-development of test and drug in EU

- IVDD classification
  - Annex II-List B (high accuracy needed for medical practice e.g. other clinical biomarkers HLA, PSA)
  - Not listed in Annex II and not intended for self-testing (most current devices, used by trained personnel)
- Location for testing
  - Clinical chemistry laboratory
  - Reference testing laboratory
  - Genetic testing laboratory
- Technology platforms validation
  - Reagent and systems

Issues discussed on PG-driven co-development of test and drug in EU

- **Overlapping data required for regulatory oversight: IVD overarching requirements for risk analysis & risk management**
  - **Design, construction, clinical validation**
  - **Technical documentation, quality assurance**
  - **Intended use**
  - **Labelling and language**
  - **False positive &/or false negative rate**
  - **Impact of test results on medical practice**

Joint VGDS/ Briefing

- **May 17, 2005: first joint EMEA/FDA VGDS briefing**
- **Videoconference**
- **Preparation**:
  - sponsor submit **data**
  - EMEA/FDA scientific review of sponsor questions
- **Pre-meeting dialogue between FDA and EMEA**
- **Sponsor presentation for interactive discussion via videoconference**
- **Final meeting report back to sponsor and in the network**
- **Further 4 sessions planned in 2006**
- **Joint EMEA/FDA public paper to describe operations (in preparation)**

ICH Brainstorming Nov 2005

- Share experience
- Create basis for pro-active harmonization
- Identify areas of differences that are important for facilitating global drug development

ICH priorities yet to be identified

Possible topics

- ✓ Definitions of terms, including implications for PG samples collection, submission format and content, and common data standards for genomic expression
- ✓ General Principles of pharmacogenomic clinical trials

Conclusions

- **EMEA road map: long term commitment in support of innovation in liaison with stakeholders**
- **New informal regulatory processes and expert panel established at the EMEA**
- **Dialogue and international co-operation essential:**

  Interaction with the European Commission

  FDA/EMEA confidentiality arrangements

  ICH

Thank you