EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Results of the EMA survey among European ethics committees (EC)

Session 4: Looking to the future: How can Ethics Committees (ECs) and Paediatric Committee / European Medicines Agency work together?

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Purpose of EMA survey

- To understand what European ethics committees have done in practice when reviewing paediatric trials with medicines
- To explore which EMA information is used *or could be useful to ECs*
- To understand how European ethics committees in general have approached reviewing paediatric trials over the last year

- Overall, to inform this meeting on working together in Europe

Description of EMA survey

- Electronic, web-based questionnaire
- September to November 2011
- Invitations (more than 800 emails) to
  - Ethics committees
  - Individual members of ethics committees
  - Ethics committees' organisations (where available)
  - Health care authorities
- Responses from 91 different participants, around 40 answered most questions
- Low response rate but we appreciated responses as snapshot

Selected results – overview

Scope of clinical trials reviewed by ECs

- Respondent ECs issued median 50 opinions last year
- Variable frequency: 1-4 to 25-50 paediatric trials per EC per year
- Usefulness of external experts for paediatric trial review: mixed
- “Paediatric trial required by PDCO”: respondent ECs were split on impact towards favourable opinion or not

How have elements of paediatric trials been assessed?

- **Assent**: systematically required by EC from which age on?
  Repeat responses for each: 6 – 8 years, 12 years, 16 years
- "Age **staggering**" (first analyse safety in older children):
  More ECs than not consider this necessary.
  A number of ECs have required age staggering when missing.
- **Risk assessment**: ECs considered "all relevant" existing study data (non-clinical, clinical adults and children), registration information, evaluated risks with uncertainties on PK/PD
- No formal approach for weighing risks implemented, but some formalism by aligning any risk with specific measure to control risk

Usefulness of guidelines?

What elements are missing in existing guidelines that would help the ethical assessment of paediatric trials by your *Ethics Committee*?

What elements are missing in existing guidelines that would *help clinical researchers* to write better protocols?

- Harmonisation of definitions (e.g., direct benefit)
- More details on practical aspects
- Infrequent response: More discussion of ethical principles

Views on information from EMA?

- EMA/PDCO Summary report or EMA Decision on PIP:
  found in 1-4 paediatric trial proposals last year by majority of ECs
- Summary report found useful, but many ECs do not know
- Sought in EMA/PDCO Summary report:
  - Existing data on medicine at time of paediatric trial (incl. risk discussion)
  - Systematic discussion of placebo use
  - Comprehensive discussion of statistical plan
  - Mentioning of blood sampling and assay volumes required by trial
  - Information on feasibility of the trial
  - Rationale of PDCO for requiring (or not) certain trials

Disagreement with elements of PIP trials?

Respondent ECs have disagreed with (decreasing frequency):

- Evaluation of the anticipated benefits and risks
- Inclusion and exclusion criteria
- Proposed placebo in trial not acceptable to participants
- *Patient information sheet, consent form, recruitment**
- Relevance of paediatric trial
- Control group

** Not specified by the PDCO in a PIP*

Interaction of ECs with EMA, bilaterally?

Which EMA information could be useful?

- Send information to ECs on new guidelines and PIPs (new, modified)
- Inform on paediatric expert workshops and their outcomes
- Infrequent answer: “Share need to discuss PIP contents”

ECs able to exchange / share? Yes,

- Inform PDCO on cases of disagreement on given paediatric trial
- Request from PDCO information on rationale when review is difficult

Which information were ECs looking for in ClinicalTrialRegister.EU?

- Medicine tested in which diseases?
- Results of paediatric trials with that medicine?
- Do other paediatric trials with the medicine exist?
- What do paediatric trials with class of medicine show?
- How many children were exposed to medicine so far?
- What are the decisions of competent authorities and / or ethics committees?

Conclusions

- Limitations of survey: not representative
- Survey useful :
  - To flag the potential of PIP documents for ECs:
    - Explicit discussion of rationale for paediatric clinical strategy
    - Explicit discussion of individual trials' methodology
    - Access to comprehensive / confidential documents may be needed
  - To suggest topics for exchange of general and specific information

  => To highlight need to have European networking of ECs on paediatrics

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Disclaimer

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