INTERNATIONALE BIOMETRISCHE GESELLSCHAFT
SOCIÉTÉ INTERNATIONALE DE BIOMÉTRIE
INTERNATIONAL BIOMETRIC SOCIETY

INTERNATIONAL BIOMETRIC SOCIETY

An International Society Devoted to the Mathematical and Statistical Aspects of Biology

DEUTSCHE REGION

To EMEA Secretariat

Prof. Dr. Joachim Röhmel
- Präsident -

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Aktenzeichen:

Comments on CPMP/ICH/5716/03 guidance document

May 26, 2005

Dear Madam/Sir,

please find enclosed comments by the German Region of the International Biometric Society on the draft Note for Guidance on Planning Pharmacovigilance activities.

We hope the drafting committee will find our comments helpful.

Yours, sincerely

(Prof. Dr. Joachim Röhmel)
- Präsident -

Comments on Draft Guideline
"ICH E2E: Pharmacovigilance Planning (PVP)"
(CPMP/ICH/5713/03, 20 November 2003)

ICH-E2E provides information on the structure and content of the Pharmacovigilance Specification and the Pharmacovigilance Plan. Specific guidance on which type of pharmacovigilance activity is appropriate under which circumstances is, however, rather limited beyond the statement that "for products for which no special concerns have arisen, routine pharmacovigilance activities might be considered adequate for the Pharmacovigilance Plan". Although it is appreciated that not in all instances more than routine pharmacovigilance is needed, it may, however, be appropriate to define more precisely, what routine pharmacovigilance means and still more information could be provided, under which circumstances more than this routine pharmacovigilance is required. Also it remains unclear what basic items a Pharmacovigilance Plan should contain if 'no special concerns have arisen'.

Section 3.3 on pharmacovigilance methods and the annex would benefit from a thorough revision including the addition of a chapter on controlled clinical trials. Particularly missing is a discussion that under some circumstances ADRs may be difficult to detect (e.g. increase in mortality in a situation where death is the expected natural course of the disease as in oncology or in stroke). This will also have methodological implications because an increase in risk will rarely be detectable outside randomised and controlled clinical trials. It is therefore of paramount importance that some discussion is included, under which circumstances spontaneous reporting systems may be insufficient and additional measurements will be needed.

Overall, a discussion of the strength of evidence obtained from the various approaches should be added (which is apparently greatest when new randomized clinical trials are performed in phase IV). The resulting hierarchy of postmarketing investigations should be coupled with clear criteria as to when the respective tools are to be used.

The structure of the Appendix is unclear: why are registries non-comparative if they are disease oriented? What is the difference between sentinel sites approach and registries? To our understanding active surveillance is part of an observational programme as contrasted to interventional studies, where again randomisation is the key part of the definition. Again those studies which have been mentioned in the fifth section of the Appendix would nicely fit into the observational section.

Finally, it should be stated that adequately trained and experienced experts from a large number of disciplines (e.g., pharmacovigilance experts, pharmacoepimiologists and biostatisticians) should be utilised for science based risk documentation and the development of appropriate Pharmacovigilance Plans, whereas the guideline currently only mentions the need for pharmacoepidemiological competence.