BRITISH HEALTHCARE BUSINESS INTELLIGENCE ASSOCIATION

Response to Concept Paper

IMPLEMENTING MEASURES IN ORDER TO HARMONISE THE PERFORMANCE OF THE PHARMACOVIGILANCE ACTIVITIES PROVIDED FOR IN DIRECTIVE 2001/83/EC AND REGULATION (EC) NO 726/2004

(PCIM/11/01 - Public Consultation on implementing measures for pharmacovigilance)

Introduction & Background

The British Healthcare Business Intelligence Association (BHBIA) aims to promote and enhance the professionalism and value of Business Intelligence within the Healthcare Industry in the UK. BHBIA members total 36 pharmaceutical manufacturers and 127 market research agencies/consultancies – including all the leading manufacturers and agencies.

The BHBIA's role involves promoting best practice in Business Intelligence. One of the ways the BHBIA does this is through mandatory adoption for members of its Legal and Ethical Guidelines for Healthcare Market Research (endorsed by The Association of the British Pharmaceutical Industry (ABPI)).

The Guidelines aim to provide all BHBIA members with clear, comprehensive and explicit best practice guidelines on the execution of healthcare market research within an up to date legal and ethical framework. These include adverse reaction reporting guidelines based upon the ABPI's Guidelines for Collecting Adverse Reactions and Product Quality Complaints from Market Research Programmes.

Given its expertise in market research and the likely impact of the adverse reaction reporting regulations upon market research studies the BHBIA would like to raise some issues and discuss these with the EMA.

The BHBIA believes that it has an important role to play supporting the development of the revised rules defining adverse reaction reporting requirements from market research.

The BHBIA fully supports that healthcare authorities need to protect patient safety and recognises the responsibility of pharmaceutical manufacturers to ensure that adverse reactions and product complaints are fully and appropriately reported.

The goal of market research is to provide objective and sound business intelligence that will inform commercial decision making. Information is collected systematically to assess (qualitatively or quantitatively) the opinions, attitudes and behaviours of the population being studied. Market research is not a commercial communication or a selling opportunity nor is it non-interventional clinical research.

Respecting respondents' rights, the confidentiality of their input and personal data and the preservation of data integrity are paramount and enshrined within the thirteen core principles of the BHBIA's Legal and Ethical Guidelines.

There are occasions within the course of a market research study when a suspected adverse reaction is mentioned or revealed and consequently a clear definition to recognise these and a workable process to report them are required.

The BHBIA would like to take the opportunity provided by the introduction of the new legislation and the accompanying legislative implementing rules to discuss definitions and processes for reporting adverse reactions from market research studies. The goal of the discussions being to ensure that effective definitions and processes are developed to make certain that adverse reaction reporting and market research are as effective as possible.

Specific Issues

Lack of Efficacy

Issue – Include only 'unexpected' lack of efficacy cases from market research

- The inclusion in 2009 of "expected" lack of efficacy (as well as unexpected) in the UK has led to an increase in reporting of unnecessary noise.
- This is due to the inclusion of cases in therapeutic areas, where there are a relatively high proportion of cases of entirely expected ineffective treatments that do not present a safety concern but are unfortunately only a reflection upon the limitations of currently available treatments foe example anti-depressants.
- In addition the reporting of cases where tolerance to the medication develops – again expected, has been inappropriately captured within the extension of the definition of lack of efficacy. Again, this reporting creates unnecessary and misleading noise.
- Furthermore this extension in the UK now seems to be contrary to the revised definition of an adverse reaction:

  (Chapter 5) Noxious and unintended effects resulting not only from the authorised use of a medicinal product at normal doses, but also from medication errors and uses outside the terms of the marketing authorisation, including the misuse and abuse of the medicinal product.

  Directive 2010/84/EU

Syndicated Data

Issue – Exclude syndicated data[1] sources as well as longitudinal databases[2] to prevent signal dilution

- Syndicated data sources are currently included in adverse reaction reporting however longitudinal patient databases are excluded.
- The Council for International Organisation of Medicinal Sciences (CIOMS) V states that there is no obligation to search through longitudinal databases for individual adverse drug reactions as this will give rise to spurious signals and conclusions.
- The same logic and reasoning applies to syndicated data sources/bases and consequently the same exclusion criteria should apply, the distinction appears illogical and artificial.

- There is concern that including syndicated data sources dilutes signal detection.

[1] Syndicated data is shared by purchasing clients i.e. it is not exclusive.
[2] Longitudinal databases are syndicated data studies repeated at regular intervals.

Reporting of reactions in patient/patients without specific identifier

Issue – Collect adverse reactions for identifiable patients

- There is confusion surrounding what constitutes a 'patient'.
- Previously the ABPI Guidelines required market researchers to forward adverse reactions that were cited in the context of an individual, identifiable patient.
- The current ABPI Guidelines require the forwarding of adverse reactions that are cited in the context of *any actual patient* or *patients w*hether or not a specific identifier is present. As a result adverse reactions cited in groups of patients and aggregated patient data now also need to be forwarded e.g. "I've seen several patients who experienced rash on Product X".
- Distinguishing between adverse reactions in groups of patients and generalisations about reactions based on feelings, hearsay or general reputation (which do not need to be forwarded) has proved difficult.
- The results are signal dilution and inappropriate reporting.

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Glossary of Market Research Terms Used

Ad Hoc Research: marketing research designed for a single specific client only carried out as a one-off project or programme of studies.

Longitudinal Data: observations of the same items collected over a period of time, the population remains constant although the sample may or may not be the same, sometimes called "time series" data.

Longitudinal Study: research study conducted over time to understand developmental trends. Can use the same or a new sample over time, generally at set intervals.

Qualitative Research: marketing research to explore opinion and value judgement of individuals from which collective general conclusions may be drawn. Such research usually involves group discussions or depth interviews (see Quantitative research).

Quantitative Research: involves the collection of samples of quantitative data large enough to allow some form of statistical analysis to be applied to the results.

Syndicated Data Services: external or independent sources of general information which may be purchased by a number of companies who may not have influenced the original design.

Syndicated Research: is where the findings and costs of a research project are shared (partially or fully) among a number of clients (who may or may not have had an input into the original design).

Specific Consultation Items

Consultation Item	Section	Topic	Concept Paper	Question
7	B.10	Audit	Audits of the quality system shall be performed at regular intervals, and not less than every two years, to assure that the quality system is in compliance with the established quality system requirements and to determine its effectiveness.	Are marketing authorisation holders required to audit the adverse reaction reporting processes that market research agencies have in place?
7	C.13	Resource management	All personnel involved in the performance of pharmacovigilance activities shall receive initial and continued training.	What are the implications for adverse reaction report training for market researchers? – Is it mandatory? – Who should supply it? – Who should sponsor it?
7	C.15	Record management	. . . . . marketing authorisation holders shall establish mechanisms enabling traceability and follow-up of adverse reaction reports while complying with data protection legislation.	If a market research respondent is not traceable because they are unwilling to provide contact details, should their adverse reaction be reported? Data protection law prohibits the passing on of personal data without permission.
8	D.18	Compliance management	Specific quality system procedures and processes shall be in place in the national competent authorities and in EMA in order to: (a) evaluate the quality; including completeness, of pharmacovigilance data submitted	What data/details would market researchers be required to supply?
14	Annex 1, 3.4	Content of electronic transmission of suspected adverse reactions	For the purpose of electronic reporting of suspected adverse reactions, Member States and marketing authorisation holders shall provide all available information on each individual case	Recording the details described is not practical in a market research setting.