The ADVANCE Code of Conduct: a tool for vaccine benefit-risk monitoring in Europe

Xavier Kurz1, Vincent Bauchau2, Jorgen Bauwens3, Phillip Bryan4, Steffen Gilsmann5, Mirna Robert-Du Ry van Beest Holle6, Raphaële Roten6, Miriam Sturkenboom7, Lieke van der Aa8, Jane Whelan9 and François Simondon10 for the ADVANCE Work Package 1

1European Medicines Agency, United-Kingdom, 2GlaxoSmithKline, Belgium, 3University Basel, Switzerland, 4MHRA, United-Kingdom, 5GlaxoSmithKline BV, the Netherlands, 6Crucell, the Netherlands, 7Erasmus University Medical Centre, the Netherlands, 8WIV-ISP, Belgium, 9IRD, France

Background

There is limited capacity in the EU to conduct large scale studies on vaccine exposure, effectiveness and safety, particularly when evaluating rare outcomes, due to:

- Difficulty to initiate and conduct multi-country studies
- Interactions between multiple stakeholders (regulators, public health agencies, academia, industry) – lack of confidence
- Funding issues –perceived conflicts of interest

The Accelerated Development of Vaccine benefit-risk Collaboration in Europe (ADVANCE) aims to establish a reliable, valid and tested framework to rapidly provide robust data and scientific evidence on vaccine benefits and risks. A Code of Conduct (CoC) aims to facilitate public private interactions while maintaining public trust.

Objective

To develop a common CoC within ADVANCE in order to:

- Speed-up initiation and conduct of vaccine studies based on previously agreed standards for governance
- Facilitate interactions between different parties based on common principles
- Support methodological excellence
- Provide confidence to health professionals and the public on results of studies conducted according to best practice.

Methods

- Review of national and international guidelines and literature to extract relevant core elements of CoC
- Recommendations critically appraised by working group to achieve consensus on elements of draft CoC.
- For each element of the CoC, agreement on:
  - Definition – Recommendations - Additional reading
  - Difference made between “must” (minimum requirement) and “should” (additional recommendation) clauses.

Initial list of guidelines consulted

- ADELFI Recommendations for professional standards and good epidemiological practices (Version 2007)
- AGENTS, DSMP and DGEpi GPS – Good Practice in Secondary Data Analysis
- EMA, Policy on the handling of conflicts of interests of scientific committee members and expert
- EMA, Guideline on good pharmacovigilance practices (GVP) Module VIII - Post-authorisation safety studies
- EMA, Guideline on good pharmacovigilance practices (GVP)-P.I: Vaccines for prophylaxis against infectious diseases
- ENCéPP, The ENCéPP Code of Conduct
- FDA, Best Practices for Conducting and Reporting Pharmacoepidemiology Safety Studies Using Electronic Health Care Data Sets
- Federation of the medical scientific associations, Code of conduct for health research
- ICMJE, Uniform Requirements for Manuscripts Submitted to Biomedical Journals
- IEA, Good Epidemiological Practice (GEP)
- ISPE, Good Pharmacoepidemiology Practices (GPP)
- Nefarma, Code of conduct on Transparency of Financial Relations
- Dutch medical associations, Code for the prevention of improper influence due to conflicts of interest
- STROBE Guidelines for reporting observational studies
- CONSORT, Consolidated Standards of Reporting Trials
- WMA, Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects

Results

Guiding principles:

Science: To rapidly deliver the best possible evidence on the research question, using appropriate scientific methods with integrity.

Public health: All decisions to conduct studies and communicate to be guided by the extent to which they serve improving the health of individuals and populations.

Transparency: Disclosure of key decisions and options taken for study design, interpretations of results and conclusions , funding sources, roles of each participant and declarations of interest.

Scientific independence: embedded in provisions of the CoC.

Draft CoC includes 9 topics and 52 recommendations:

- **Scientific integrity** (1-3): Acting in accordance with the values of science, such as truthfulness, honesty and open reporting, even when no one is looking over the researcher’s shoulder
- **Transparency** (4-11): Having study information accessible to all, incl. registration of study and protocol in public database, sources of funding, declarations of interest (DoIs), recommendations of scientific advisory board, study report.
- **Conflicts of interest** (12-14): Situation in which a person involved in a research project has a professional or personal interest sufficient to influence the objective exercise of his/her judgment towards any activity of the project; DoIs to be disclosed, potential CoIs to be identified and addressed.
- **Study protocol** (15-24)
- **Study report** (24-31)
- **Publications and scientific communications** (32-37):
  - To be agreed in advance and included in research contract; PI’s freedom to publish irrespective of funding source; requester/funder entitled to comment; all study results to be made available; regulatory/public health authorities to be rapidly informed.
- **Subject privacy** (38-40)
- **Sharing of study data** (41-48): After the study report is finalised: open and collaborative approach to data sharing based on a request justifying interest for public health and acceptance at appropriate study governance level; provisions of CoC apply to data requester and data analyses.
- **Research contract** (49-52): Key elements are clarity and transparency; proposal for list of elements to be included ; research contract should specify if study follows provisions of CoC or accepted guidelines(s).

Conclusions

- Multistakeholder approach
- Elements of CoC developed based on key Guiding principles
- Good Practice Guidance to include recommendations on CoC, governance models, quality management and communications.
- Work in progress; public consultation to be initiated in September 2015 and agreement to be sought from all parties involved in vaccines B/R studies
- Relevance beyond the field of vaccines

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