Opportunities and challenges of ADVANCE best practice solutions: regulatory perspective

EU Ecosystem for monitoring of post-licensure vaccine benefit and risk: from ADVANCE to VAC4EU

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An agency of the European Union

What do regulators need?

Easy access to valid real-world evidence to support regulatory decisions on vaccines (e.g. safety, efficacy, benefit-risk monitoring)

What is expected from RWE?

Evidence is:

- adequate (e.g. precision, adequate range of characteristics of population covered, length of follow-up derived from)

- derived from real-data sources of demonstrated good quality

  - consistency, completeness, accuracy, timeliness

- valid (internal and external validity)

- consistent (across countries/data sources) - or differences can be explained

Currently, use of RWE by regulators faces many challenges:

➢ Operational

- Feasibility
- Governance
- Sustainability

➢ Technical

- Extent of data collected
- Data completeness
- Appropriate terminologies and data formats
- Potential for data linkage
- Consistent, accurate and timely data collection and management

➢ Methodological

- Variability in results from multi-data source studies
- Understanding the data source environment
- Adequate data collection and analysis on potential confounders and effect modifiers

How does the ADVANCE public-private partnership contribute to OPTIMAL solutions for RWE on vaccines?

Operational

- Landscaping of potential data sources

- Long-term funding for data infrastructures

- Published documentation of data source characteristics and policy for collaboration and data sharing

- Management of access in line with GDPR and national legislation

- Data anonymisation processes where required

- Data sharing agreements at study inception

- Use of ENCePP Code of Conduct

Operational

- Landscaping of potential data sources √ AIIR survey + D3.4. Metaprofile of data sources

- Long-term funding for data infrastructures √ D7.7 ADVANCE Blueprint

- Published documentation of data source characteristics and policy for collaboration and data sharing √ D3.5. Procedures for data access, sharing, linkage and integration

- Management of access in line with GDPR and national legislation √ D3.5 Privacy and ethics

- Data anonymisation processes where required √ D3.5.

- Data sharing agreements at study inception √ D1.10 Good Practice Guidance Module 2: Governance models.

- Use of ENCePP Code of Conduct √ D 1.9 - Good Practice Guidance – Modules 1 and 3: Code of Conduct and Quality recommendations

ADVANCE Code of Conduct: framework for public-private partnership

Review

The ADVANCE Code of Conduct for collaborative vaccine studies

Xavier Kurz [a,*], Vincent Bauchau [b], Patrick Mahy [c], Steffen Glismann [d], Lieke Maria van der Aa [c], François Simondon [e], for the ADVANCE consortium [1]

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Core principles:
- Best science
- Strengthening public health
- Transparency

Stand-alone recommendations to facilitate collaboration between multiple partners of collaborative vaccine benefit-risk studies

Table 1. Recommendations from the ENCePP Code of Conduct, the ISPE Guidelines for Good Pharmacoepidemiology Practice (GPP) and the ADVANCE Code of Conduct for post-autorisation studies.

Topics	ENCePP Code of Conduct	ISPE Guidelines for Good Pharmacoepidemiology Practice (GPP)	ADVANCE Code of Conduct
Objective	To support scientific independence and transparency throughout the research process; to strengthen the confidence in the integrity and value of the research	To help ensure the quality and integrity of research; to facilitate transparency and ethical integrity	To support effective collaborations and clear governance for the conduct of collaborative post-authorisation vaccine studies
Scope	Non-interventional post-authorisation studies	All types of pharmacoepidemiological (PE) research	Post-marketing vaccine benefit-risk monitoring activities
Guiding principles	Scientific independence and transparency	Sound PE research, framework for conducting and evaluating PE studies, appropriate utilisation of technical resources, transparency, ethical integrity	Best science, strengthening public health, transparency
Participants	Protocol developed by individuals with appropriate	Personnel should have education, training or	All study team members to be qualified and to act in

Source: The ENCePP Code of Conduct: a best practice for scientific independence and transparency in non-interventional post-authorisation studies. *Rosa Gini et al. PDS, in press*

ADVANCE CoC: unique source of guidance on collaborative pharmacoepidemiological research in Europe

Technical

- Use of common data elements, data formats and terminologies, or mapping to international system

- Partial or full data mapping to CDM including routine validation process

- Quality assurance and control procedures – indicators of data quality

- Internal or external data audit -

- Benchmarking to external data source

- EU Qualification procedure for data source

Technical

- Use of common data elements, data formats and terminologies, or mapping to international system √ D3.3 Technical Requirements Analysis - D5.5 Vaccine ontology report - CodeMapper

- Partial or full data mapping to CDM including routine validation process √ D5.6 Results of POC -phase 1 studies

- Quality assurance and control procedures – indicators of data quality √

- Internal or external data audit – D1.10: Governance models.

- Benchmarking to external data source √ D5.6 Results of POC -phase 1 studies

- EU Qualification procedure for data source **to be considered?**

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Methodological

- Detailed description of study design and data collected in data sources

- Documentation of feasibility analyses

- Registration of study in public database, with study protocols and results

- Use of best methodological standards in statistics and epidemiology

- Use of EU Scientific Advice procedure

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Benefit–Risk Monitoring of Vaccines Using an Interactive Dashboard: A Methodological Proposal from the ADVANCE Project

Kaatje Bollaerts[1] · Tom De Smedt[1] · Katherine Donegan[2] · Lina Titievsky[3] ·
Vincent ...[4]

PLOS ONE

Bias due to differential and non-differential disease- and exposure misclassification in studies of vaccine effectiveness

Tom De Smedt[1], Elizabeth Merrall[2], Denis Macina[3], Silvia Perez-Vilar[4,5], Nick Andrews[6], Kaatje Bollaerts[1]*

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Review

The benefit of the doubt or doubts over benefits? A systematic literature review of perceived risks of vaccines in European populations

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Methodology for computing the burden of disease of adverse events following immunization

Scott A. McDonald[1] | Danielle Nijsten[1] | Kaatje Bollaerts[2] | Jorgen Bauwens[3,4] | Nicolas Praet[5] | Marianne van der Sande[1,6] | Vincent Bauchau[5] | Tom de Smedt[2] | Miriam Sturkenboom[2,7] | Susan Hahné[1]

BMC Medicine

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Application of real-time global media monitoring and 'derived questions' for enhancing communication by regulatory bodies: the case of human papillomavirus vaccines

Priya Bahri[1,2*], Julianna Fogd[2], Daniel Morales[2,3], Xavier Kurz[2] and on behalf of the ADVANCE consortium

Rosa Gini, Caitlin Dodd, Kaatje Bollaerts, Claudia Bartolini, Giuseppe Roberto, Consuelo Huerta, Elisa Martin, Talita Duarte Salles, Gino Picelli, Lara Tramontan, Benedikt Becker, Charlotte Switzer, Sonja Banga, Jorgen Bauwens, Daniel Weibel, Miriam Sturkenboom (2017) **Algorithms to identify pertussis in four European primary care databases - the ADVANCE project.** ISPE 2017 (Oral presentation)

Kaatje Bollaerts, Alexandros Rekkas, Tom De Smedt, Caitlin Dodd, Nick Andrews, Rosa Gini (2017) **Analytical interrelations between validity indices for validation of case-finding algorithms in healthcare data research: a contribution from ADVANCE.** ISPE 2017 (Oral presentation)

Elizabeth Merrall, Denis Macina, Silvia Perez-Vilar, and Kaat Bollaerts (2016) **Disease and exposure misclassification in studies of vaccine effectiveness: a simulation tool.** Poster presented at ISPE 2016

Conclusions

✓ ADVANCE solutions respond to most operational, technological and methodological challenges for using RWD for regulatory purposes

✓ Processes are in place to evaluate and address issues of quality <u>prior</u> to data analysis

✓ PPPs have strengths and weaknesses but the ADVANCE governance and Code of Conduct can support confidence in results based on strong principles (science, public health, transparency)

✓ Some questions remain:

  ✓ Number and characteristics of databases able to meet inclusion criteria
  ✓ Number of vaccines identified and monitored in proof-of-concept studies
  ✓ Demonstration of usability of ADVANCE solutions in real life

Thank you for your attention

Further information

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