IMDRF MDCE WG Comment Form		Document:IMDRF MDCE WG(WD2)/Nx (formerly GHTF/SG5/N4:2010) Post-Market Clinical Follow-Up Studies						
Name	**Company/Organization**	**Email Address**	**Section**	**Line Number**	**Type of Comment**	**Comment**	**Proposed Change**	**Resolution**
International Society for Pharmacoepidemiology (ISPE)	ISPE	info@pharmacoepi.org	1.0	51	Definition and clarity	PMCF is language used in EU but not necessary in other countries. Thus, it is unclear what other postmarketing requirements would fall under this guidance (e.g., would US FDA PAS and 522 be included? What about postmarketing studies from other jurisdictions?) Does clinical performance include product goals?	Clearly state what PMCF covers in this document and distinguish between PMCF and PMS. Define all postmarketing requirements in each jurisdiction which are covered by each (overarching PMS and specific PMCF). Ideally, include a table which defines each type of study, definition, and distinguishing factors from other studies/efforts across all IMDRF members and observers.	
ISPE	ISPE	info@pharmacoepi.org	5.0	173	Clarity needed	Unclear how to distinguish when PMCF would and would not be necessary	Recommend guidance on how MAH could make these determinations and clarification of how determinations are made by regulators.	
ISPE	ISPE	info@pharmacoepi.org	6.0	177-188	Additional element needed	Transparency of the process is one of the critical components in scientific investigation but not currently mentioned or emphasized in the document	Recommend that the document clearly states that protocols and results needed to be transparent and publicly available for clinicians and scientific community, and in also be available in plain language for patients (i.e., layman's summary).	

IMDRF MDCE WG Comment Form		Document:IMDRF MDCE WG(WD2)/Nx (formerly GHTF/SG5/N4:2010) Post-Market Clinical Follow-Up Studies						
Name	**Company/Organization**	**Email Address**	**Section**	**Line Number**	**Type of Comment**	**Comment**	**Proposed Change**	**Resolution**
ISPE	ISPE	info@pharmacoepi.org	6.0	187	Modification	Not always appropriate to implement the study according to the initial plan. New information may become apparent during the process or the clinical contexts and practice may change as the study is being implemented. In both cases, what is important is to clearly state and provide justifications for necessary change. Again, transparency is needed.	Acknowledge that it is not always appropriate or required to implement the study according to the initial plan and emphasize need for rationale/justification and transparency (i.e., update of protocol registration) when deviating from initial plan.	
ISPE	ISPE	info@pharmacoepi.org	6.2	192-204	Clarity needed	Both study designs and data sources need to be covered in more comprehensive fashion.	Include explicit language to cover the following: randomized designs, prospective vs retrospective, surveys, new data collection vs use of secondary data. In line 203, recommend explicit language regarding data sources (e.g., claims, EHR).	
ISPE	ISPE	info@pharmacoepi.org	6.2	215-216	Clarity needed	Need to justify design and methods are adequate to address research question	Add justification of design to address research question as a factor to consider	
ISPE	ISPE	info@pharmacoepi.org	6.2	221	Modification	Device exposure not included	Add clear definition and justification for device exposure group	
ISPE	ISPE	info@pharmacoepi.org	6.2	217-235	Clarity needed	Unclear how comparative vs. descriptive nature of study is delineated	Add specific factor for whether design is comparative or descriptive	
ISPE	ISPE	info@pharmacoepi.org	6.2	228	Clarity needed	Adjudication/validation not covered (in this section or appendix)	Add discussion of adjudication/validation, when each is needed, and what to include in adjudication and validation of data elements	

IMDRF MDCE WG Comment Form		Document: IMDRF MDCE WG(WD2)/Nx (formerly GHTF/SG5/N4:2010) Post-Market Clinical Follow-Up Studies						
Name	**Company/Organization**	**Email Address**	**Section**	**Line Number**	**Type of Comment**	**Comment**	**Proposed Change**	**Resolution**
ISPE	ISPE	info@pharmacoepi.org	6.2	232	Clarity needed	Propensity scores are not listed as viable option for confounding adjustment	Include propensity scores within listing of appropriate analytical methods for confounding adjustment.	
ISPE	ISPE	info@pharmacoepi.org	6.2	233-235	Clarity needed	Sensitivity analyses for biases not included	Add sensitivity analyses as design consideration	
ISPE	ISPE	info@pharmacoepi.org	6.2	233-235	Clarity needed	Assessment of misclassification not included	Add evaluation of misclassification (as appropriate) for exposure, outcome, and key covariates	
ISPE	ISPE	info@pharmacoepi.org	6.2	240	Modification	The sentence implies that matching is always the optimal strategy, but the optimal analytic strategy depends on various factors including the study question, design and data sources.	Recommend not implying that matching is always the optimal strategy. Instead, language such as “control sampling strategy, e.g., matching” is recommended.	
ISPE	ISPE	info@pharmacoepi.org	6.3	243-244	Modification	Sometimes appropriate to adjust original study plan (e.g., for unexpected findings and situations)	Recommend allowance for study plans (e.g., protocol) to be adjusted, with provision of clinical, practical and methodological justifications for any adjustment to the plan and emphasize the need for transparency	
ISPE	ISPE	info@pharmacoepi.org	6.3	242-254	Additional element needed	Registration and transparency not included	Add study registration as a factor to consider during study implementation	
ISPE	ISPE	info@pharmacoepi.org	6.3	252-254	Harmonization	Harmonization and recommendation on reporting structure (e.g., template/outline) from IMDRF is warranted.	Recommend that IMDRF provide proposed structure (template/outline/format) to be used for all PMCF (and similar) study reports.	
ISPE	ISPE	info@pharmacoepi.org	6.3	252-254	Additional element needed	No comment on publication	Add publication as element to consider in implementation	

IMDRF MDCE WG Comment Form		Document:IMDRF MDCE WG(WD2)/Nx (formerly GHTF/SG5/N4:2010) Post-Market Clinical Follow-Up Studies						
Name	**Company/Organization**	**Email Address**	**Section**	**Line Number**	**Type of Comment**	**Comment**	**Proposed Change**	**Resolution**
ISPE	ISPE	info@pharmacoepi.org	Appendix C	440-444	Additional information	Add other guidelines	Add ISPE GPP, ISPE/ISPOR transparency framework (#1 and #2 below). Further, recommend addition of checklist similar to ENCePP protocols and reference to ENCePP methodological guide (http://www.encepp.eu/standards_and_guidances/index.shtml). 1. International Society for Pharmacoepidemiology. Guidelines for Good Pharmacoepidemiology Practices (GPP). Pharmacoepidemiol Drug Saf. 2016;25:2-10. 2. Wang SV, Schneeweiss S, Berger ML, et al. Reporting to Improve Reproducibility and Facilitate Validity Assessment for Healthcare Database Studies V1.0 [published correction appears in Pharmacoepidemiol Drug Saf. 2017	