Name of organisation or individual*	Line from* (line Nr or 0 for general comment)	Line to* (line Nr or 0 for general comment)	Section number	Comment and rationale (to go to next line within the same cell use Alt + Enter)	Proposed changes / recommendation (if applicable - to be used if you want to propose specific text changes)
Health Action International	35	35	Main technical issues to be addressed	This reference is missing in the bibliography. If it is this paper, which we suspect: https://ascpt.onlinelibrary.wiley.com/doi/full/10.1002/cpt.2480 --> the authors are from Pfizer. ICH/EMA should reference a more objective source.	Replace reference with a more objective source.
Health Action International	36	42	Main technical issues to be addressed	Other challenges of RWD stem from ethical concerns around data collection practices and privacy. In addition to data validity, data representativeness is an issue for RWD.	Add '*and data collection practices and privacy*' after data source characteristics in this sum up. Add '*data representativeness*' after data validity in this sum up.
Health Action International	42	44	Main technical issues to be addressed	The diverse nature of RWD as characterised above, makes this case-by-case analysis crucial. RWD will also often not be the best source of data to answer certain questions.	Clarify that a case-by-case analysis of suitability of RWD is crucial given the diverse nature of RWD and its quality.
Health Action International	69	71	Main technical issues to be	Effectiveness testing happens before market-authorisation. Using RWE (essentially observational data) for effectiveness studies poses serious risks and should not replace RCT study designs.	Acknowledge the limitations of RWE in effectiveness testing.

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			addressed		
Health Action International	79	81	Main technical issues to be addressed	This sentence seems incomplete. How will common understanding of terminology on RWD/RWE drive access to innovative medicines? For other harmonisation efforts of ICH, it is not proven that they drive access to innovative medicines, but, due to the industry-driven nature of ICH, that there's actually a risk of watering down standards (see: https://www.sciencedirect.com/science/article/abs/pii/S0277953602003398?via%3Dihub).	Critically revise this sentence, as the link between better terminology and access to innovative medicines is unclear, also back this statement with (objective) evidence.
Health Action International	88	89	Objectives and potential benefits	But RWE won't always be suited to do this. Add as aim: with strong safeguards to protect standards of evidence in regulatory decision-making.	Add to this sentence: '*with strong safeguards to protect standards of evidence in regulatory decision-making.*'
Health Action International	Table after line 91, second row, objective. Bullet 1 "agree on common principles…"		Objectives and potential benefits	Because ICH is largely industry driven, the EMA should ensure the possibility to come up with additional criteria and requirements to ensure use of RWE will never water down standards of evidence.	
Health Action International	Table after line 91, second row, objective. Bullet 1 "agree		Objectives and potential	The use of RWD/RWE cannot be seen independently from how it has been analysed and processed. Especially if advanced data analytics are used, there are some risks. Therefore, emphasise its protocols for RWD/RWE as well as the methods of analysis for evidence generation.	Include '*reporting of data analysis, including analyses using machine learning, in protocols.*'

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	on common principles…"		benefits		
Health Action International	Table after line 91, second row, objective. Bullet 2 "promote transparency by…"		Objectives and potential benefits	Now it seems voluntary. Transparency efforts are usually only effective when they are compulsory. Public transparency on use of RWD should be an obligation, through registration in publicly available and accessible registries.	Rephrase objective to make obligatory transparency the aim.
Health Action International	95	97	Objectives and potential benefits	Something that should not be overlooked is best practices for data collection. During data collection one has a lot of influence on data quality. By adding a focus on high-quality data collection, many challenges later on can be avoided, and the utility of RWD will be increased. This approach, although not easy, better addresses the root cause of poor-quality data and is therefore potent in reaching high standards of RWE. Also, there are many exploitative data collection practices, which should be actively combatted and avoided for RWE in medicines regulation.	Include: "best practices for data collection" as priority.
Health Action International	117	119	Important considerations	All efforts should be centred around protecting standards of evidence. By extensively analysing risks of use of low-quality or biased data and installing comprehensive safeguards to prevent deterioration of evidence standards. Again, the link between harmonisation of RWE terminology and access to innovative treatments is again not clear.	Emphasise importance of protecting standards of evidence.

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