

30 June 2023  
EMA/CHMP/ICH/295401/2023  
Committee for Human Medicinal Products

## ICH Reflection paper on proposed international harmonisation of real-world evidence terminology and convergence of general principles regarding planning and reporting of studies using real-world data, with a focus on effectiveness of medicines

|                                 |                   |
|---------------------------------|-------------------|
| Transmission to CHMP            | 30 June 2023      |
| Adoption by CHMP                | 30 June 2023      |
| Release for public consultation | 30 June 2023      |
| Deadline for comments           | 30 September 2023 |

Comments should be provided using this [template](#). The completed comments form should be sent to [ich@ema.europa.eu](mailto:ich@ema.europa.eu)



1 **ICH Reflection Paper**  
2

3 **International Harmonisation of Real-World Evidence Terminology and Convergence of**  
4 **General Principles Regarding Planning and Reporting of Studies Using Real-World Data, with**  
5 **a Focus on Effectiveness of Medicines**

6 *Under public consultation until 30 September 2023*

7 **Introduction**

---

8 The role of real-world data (RWD) and real-world evidence (RWE) in supporting the evaluation of  
9 medicines across the different stages of their development and lifecycle-is evolving [Framework for  
10 FDA, United States' Real-World Evidence Program 2018; Optimizing the Use of Real World Evidence  
11 to Inform Regulatory Decision-Making, Health Canada, Canada's 2019; ENCePP Guide on  
12 Methodological Standards in Pharmacoepidemiology, EMA 2022].

13 In July 2022, the International Coalition of Medicines Regulatory Authorities expressed its strong  
14 support to strengthening international collaboration on activities to enable the use of RWE in regulatory  
15 decision-making [ICMRA, 2022]. This statement emphasises the engagement of regulatory agencies  
16 across the globe to address current gaps due to the lack of standardisation of RWD/RWE terminology  
17 and formats, the heterogeneity of data quality across RWD sources, and the various study designs used  
18 depending on the types of diseases, medicines, and regulatory context. Addressing these challenges  
19 should be supported by common definitions and best practices.

20 This Reflection Paper outlines a strategic approach for ICH to address some of these challenges. The  
21 goal is to further enable the integration of RWE into regulatory submissions and timely regulatory  
22 decision-making.

23 **Main technical issues to be addressed**

---

24 Recognising that traditional randomised clinical trials (RCTs) are foundational for generating evidence  
25 on safety and effectiveness pre-authorisation, under appropriate circumstances other approaches can  
26 generate evidence suitable for regulatory decision-making. For example, RWE can be generated by  
27 using RWD to ascertain endpoints in point-of-care RCTs or serve as a comparator arm in an externally  
28 controlled trial (including historically controlled trials)[Framework for FDA, United States' Real-  
29 World Evidence Program (2018)]. RWD are also used in non-interventional studies [FDA  
30 Considerations for the Use of Real-World Data and Real-World Evidence To Support Regulatory  
31 Decision-Making for Drug and Biological Products (2021)], for example to analyse the utilisation of an  
32 authorised medicine in routine medical practice, and to generate evidence that supports regulatory  
33 decisions on (long-term) post-marketing safety and effectiveness of medicines [Jonker et al., 2022;  
34 Flynn et al., 2022]. RWD can be used to better understand current treatment patterns, co-morbidities,  
35 and disease prognosis [Dagenais et al., 2022].

36 Nevertheless, several challenges exist, including the heterogeneity of RWD types (e.g., electronic health  
37 records, registry data, claims data, longitudinal drug prescriptions, dispensing or other drug utilisation  
38 data, patient-generated data), healthcare settings (e.g., primary/secondary/tertiary cares, self-treatable  
39 conditions), data source characteristics (e.g., purpose, population coverage, data elements, coding  
40 terminology), levels of data quality and data validity, and a variety of governance models for data

41 sharing and access [Bakker et al., 2022; Morton et al., 2016], emphasised by distinct national/regional  
42 laws and regulations. The suitability of RWD to generate adequate evidence to support regulatory  
43 applications currently requires a case-by-case analysis, which may be driven by different criteria related  
44 to the aforementioned factors and depending on the research question(s).

45

46 There are currently no internationally harmonised definitions of RWD and RWE.

47 • The Framework for FDA, United States’ Real-World Evidence Program (2018) defines RWD as  
48 *“the data relating to patient health status and/or the delivery of health care routinely collected*  
49 *from a variety of sources”*, and RWE as *“clinical evidence regarding the usage and potential*  
50 *benefits or risks of a medical product derived from analysis of RWD. RWE can be generated by*  
51 *different study designs or analyses, including but not limited to, randomised trials, including*  
52 *large simple trials, pragmatic trials, and observational studies (prospective and/or*  
53 *retrospective)”*.

54 • RWD has been defined in an EU-led publication as *“routinely collected data relating to a*  
55 *patient’s health status or the delivery of health care from a variety of sources other than*  
56 *traditional clinical trials”*, and RWE as *“the information derived from the analysis of RWD”*  
57 [Cave et al., 2019].

58 Although these definitions (and others such as from learned societies, other regulators, etc.) are similar,  
59 the terms RWD and RWE are nonetheless used inconsistently and interchangeably [Concato et al.,  
60 2020; Concato & Corrigan-Curay, 2022; ENCePP, 2022]. Applying different definitions has limited  
61 convergence of best practices among regulators.

62 Recently published studies have attempted to measure the frequency of use of RWD/RWE in medicine  
63 approvals and the extent of use for decision-making [Flynn et al., 2022; Purpura et al., 2021; Eskola et  
64 al., 2021]. Variable interpretation of definitions, heterogenous ways of describing and characterising  
65 RWD sources, and diverse methodologies used in these studies have led to a different estimated number  
66 of medicines’ applications including RWD/RWE. While a significant and increasing proportion of  
67 marketing authorisations contain RWE, these observed discrepancies may lead to different levels of  
68 acceptance of what is considered to be RWD/RWE across jurisdictions.

69 Whilst the contribution of what is now called RWD and RWE has long been recognised for safety  
70 monitoring and disease epidemiology across medicines’ lifecycles, their use to demonstrate  
71 effectiveness is more nascent. Additional work is needed for an in-depth analysis of the actual  
72 contribution of RWE to regulatory decision-making, why such information was not considered adequate  
73 in some cases, and how it contributed to the approval in other cases. This work would also help  
74 complement existing recommendations to medicines developers on the submission of RWE (see the  
75 Annex including Regulatory Agencies guidance on RWD/RWE as well as the following publications  
76 [Simpson et al., 2022 (part 4); Kent et al., 2021; Griesinger et al., 2022; Simpson et al., 2022 (part 8);  
77 Jaksa et al., 2021; Angelis et al., 2018]).

78 National/regional laws and regulations can present challenges to convergence and harmonisation of  
79 terminology and convergence of guidance related to RWD/RWE. However, reaching common  
80 understanding at international level on terminology and how RWD/RWE can reduce gaps in knowledge  
81 for new and existing medicines, and would help drive forward access to innovative medicines.

## 82 Objectives and potential benefits

83 The objectives of this Reflection Paper are:

- 84
- 85 • To engage ICH on convergence of terminology for RWD and RWE, on the format for protocols and reports of study results submitted to regulatory agencies throughout the lifecycle of medicinal products, and on promoting registration of protocols and reports;
  - 86
  - 87 • To inform the assessment of RWD and RWE for regulatory purposes.

88 The ultimate benefit of this work is expected to be higher quality RWE that can substantively contribute to the body of evidence supporting the benefit and risk decision-making on medicines.

90 The following stepwise harmonisation approach is proposed, with the scope and focus to be reassessed prior to initiating the work:

|    | Topic   | Objective   | Deliverables   | Tentative timeframe  |
|----|---|---|--|--|
| 1. | <b>RWD/RWE terminology, metadata, and assessment principles</b>     | <ul style="list-style-type: none"> <li>• Promote a common understanding of the types and scope of RWD/RWE</li> <li>• Guide the discoverability, identification, and description of RWD</li> <li>• Inform the assessment of RWD/RWE for regulatory purposes</li> </ul>   | <ul style="list-style-type: none"> <li>• Common operational definitions of RWD and RWE, with clear scope, breadth of potential RWD sources, and level of granularity (e.g., pertaining to RCTs and non-interventional studies)<sup>1</sup></li> <li>• Core list and use of metadata</li> <li>• General principles for assessment of RWD/RWE</li> </ul> | Submit new ICH topic proposal in Dec 2023 or Dec 2024                              |
| 2. | <b>RWD/RWE protocol &amp; report format, and study transparency</b> | <ul style="list-style-type: none"> <li>• Agree on common principles regarding formats for RWD/RWE protocols and reports of study results submitted to regulators</li> <li>• Promote transparency by encouraging registration of study protocols and study reports in publicly available registries</li> </ul> | <ul style="list-style-type: none"> <li>• Principles for structure and content of protocols and reports (for medicines developers)</li> <li>• Recommended “best practices” for registration of study protocols/results</li> </ul>   | Initiate work after the first guideline reaches <i>Step 4</i> of the ICH Procedure |

92 This Reflection Paper represents the initial step of an incremental approach towards harmonisation of regulatory RWE guidance. The following topics could be considered priorities for subsequent ICH guidelines, based on stakeholders’ feedback:

- 95
- Best practices for data quality;

<sup>1</sup> Reference to the ICH M14 glossary will be made during development of the Concept Paper.

- 96           • Data standards for RWD;  
97           • Appropriate application of study designs and data analyses.

98    **Important considerations**

---

99    *Stakeholders and consultation*

100   The complexity of use and impact of RWD/RWE in medicines regulation raise numerous challenges,  
101   and the need for involvement of all concerned stakeholders is therefore acknowledged. Should this  
102   Reflection Paper be endorsed by ICH, a public consultation is proposed based on the learnings from  
103   other ICH guidelines such as ICH E6(R3), ICH E8, and ICH E17 to ensure that all relevant parties are  
104   informed and given the opportunity to bring forward their views on technical and operational aspects  
105   to be considered when addressing harmonisation of the different focus areas described above. Following  
106   the proposed global public consultation on this Reflection Paper and as the guideline work progresses,  
107   the Concept Paper and Business Plan should include strategies for extended public consultation and  
108   engagement.

109   *Benefits of ICH harmonisation*

110   This proposal will aim to benefit all types of medicinal products at any stage of their lifecycle, i.e., from  
111   development/pre-approval to post-marketing monitoring. ICH guidance can increase the efficiency of  
112   resources across a large number of stakeholders, by aligning expectations of medicines regulators,  
113   medicines developers/pharmaceutical industry, patient advocacy groups, contract research  
114   organisations, academia, and other stakeholders using RWD to generate evidence on medicinal  
115   products.

116   By supporting the delivery of a regulatory system able to integrate RWE in a more harmonised way  
117   into submissions for medicines approval and decision-making, this proposal can support timely  
118   decisions on the development of innovative treatments, help to address unmet medical needs and  
119   support the safe and effective use of medicines.

120   *Interface with existing and upcoming guidances (see Annex)*

121   Several initiatives have been launched in different regions, including but not limited to Europe, the  
122   United States and Canada, to evaluate and enable the use of RWE across the spectrum of regulatory use  
123   cases that will ultimately lead the development and utilisation of medicines for patients. In December  
124   2018, FDA, United States published a [RWE Framework](#) to address current challenges in using RWD  
125   and RWE. This was followed by a [series of RWD/RWE draft guidances in 2021, a final guidance on  
126   submitting documents utilising RWD/RWE in 2022, and a draft guidance on externally controlled trials  
127   in 2023](#). Health Canada is also working towards optimising the use of RWE to inform regulatory  
128   decision-making as described in a [Health Products and Food Branch Notice](#), first published in April  
129   2019. In 2020 the [HMA/EMA Big Data Task Force](#) issued [ten priority recommendations](#) linked to  
130   human medicines, related to DARWIN-EU, including the development of the European Medicines  
131   Regulatory Network [Data Standardisation Strategy](#) to allow convergence with partners on standards  
132   and guidelines linked to Big Data and RWE. All these initiatives will support the development of the  
133   proposed new ICH guidelines.

134   Synergies and complementarities are foreseen with other ICH guidelines, for example E6(R3) and its  
135   Annex II, ICH M14, as well as ICH M11, currently under development. The ICH guideline M14 on  
136   “*General principles on planning and designing pharmacoepidemiological studies that utilize real-*

137 *world data for safety assessment of a medicine*” focuses on convergence of guidance and best practices  
 138 across jurisdictions on planning and designing safety studies that use RWD, whereas the potential for  
 139 RWE can be broadened to include assessing the effectiveness of medicines and analysing utilisation of  
 140 marketed medicines administered in routine medical practice. The ICH guideline M11 on “*Clinical*  
 141 *electronic Structured Harmonised Protocol (CeSHarP)*” covers general protocol design principles and  
 142 approach used to develop the separate associated documents, i.e. the ICH M11 Clinical Electronic  
 143 Structured Harmonised Protocol Template and the Technical Specification, that are acceptable to all  
 144 regulatory authorities of the ICH regions. The scope of the M11 guideline focuses on protocol of clinical  
 145 trials only, whereas RWD have been used mostly in non-interventional studies. The proposed guideline  
 146 2 includes the convergence of structure of study reports in addition to study protocols.

147 Efforts will be needed to ensure that duplications are minimised, and that knowledge gathered from  
 148 existing projects are leveraged to the maximum so that we can build on lessons learnt.

149 Recognising the need to leverage the relevant expertise (e.g., pharmacoepidemiology, biostatistics,  
 150 regulatory science) within regulatory authorities and medicines developers to undertake this initiative,  
 151 and to leave enough time for the maturation of guidances under development, a long-term plan with a  
 152 stepwise approach is suggested. This strategy will help effectively progress towards harmonisation of  
 153 terminology related to RWD and RWE and best practices while ensuring complementarity of scope  
 154 between the new and existing guidelines.

#### 155 **Annex – Regulatory initiatives and guidances related to RWD/RWE**

---

156

157 The following table provides examples of existing regulatory initiatives and guidances related to RWD  
 158 and RWE. It does not constitute a complete inventory of planned or ongoing activities across  
 159 jurisdictions. In addition, there are many other non-regulatory initiatives and guidances that will be  
 160 considered as this work progresses (e.g., from learned societies and other relevant projects and  
 161 stakeholders).

| Jurisdictions          | Regulatory Initiatives and Guidances   | Links  |
|------------------------|--|--|
| EC, Europe<br>(EMA-EC) | Joint HMA/EMA Big Data Initiative, including: <ul style="list-style-type: none"> <li>• Darwin EU</li> <li>• Data quality framework for EU medicines regulation</li> <li>• Metadata list describing real-world data sources and studies</li> <li>• Good practice guide for the use of the Metadata Catalogue of Real-World Data Sources</li> <li>• Data standardization strategy</li> </ul>           | <a href="#">LINK</a>   |
|                        | Other Guidances: <ul style="list-style-type: none"> <li>• CHMP guideline on registry-based studies</li> <li>• ENCePP Code of Conduct</li> <li>• ENCePP Guide on Methodological Standards in Pharmacoepidemiology</li> <li>• Good pharmacovigilance practices (GVP) Module VIII of post-authorisation safety studies</li> <li>• Scientific guidance on post-authorisation efficacy studies</li> </ul> | <a href="#">LINK</a><br><a href="#">LINK</a><br><a href="#">LINK</a><br><a href="#">LINK</a> |
| FDA, United States     | Framework for FDA, United States’ Real-World Evidence Program (2018)   | <a href="#">LINK</a>   |

| Jurisdictions                  | Regulatory Initiatives and Guidances   | Links                |
|--------------------------------|--|----------------------|
|                                | Individual Guidances: <ul style="list-style-type: none"> <li>• Assessing Electronic Health Records and Medical Claims Data To Support Regulatory Decision-Making for Drug and Biological Products</li> <li>• Assessing Registries to Support Regulatory Decision-Making for Drug and Biological Products</li> <li>• Considerations for the Use of Real-World Data and Real-World Evidence to Support Regulatory Decision-Making for Drug and Biological Products</li> <li>• Data Standards for Drug and Biological Product Submissions Containing Real-World Data</li> <li>• Submitting Documents Utilizing Real-World Data and Real-World Evidence to FDA for Drugs and Biologics</li> <li>• Use of Electronic Health Records in Clinical Investigations</li> <li>• Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices</li> <li>• Considerations for the Design and Conduct of Externally Controlled Trials for Drug and Biological Products</li> </ul> | <a href="#">LINK</a> |
| <b>Health Canada, Canada</b>   | Optimizing the Use of Real World Evidence to Inform Regulatory Decision-Making   | <a href="#">LINK</a> |
|                                | Elements of real world data/evidence quality throughout the prescription drug product life cycle   | <a href="#">LINK</a> |
|                                | DRAFT CADTH Real-World Evidence Reporting Guidance   | <a href="#">LINK</a> |
| <b>MHRA, UK</b>                | Guidance on the use of real-world data in clinical studies to support regulatory decisions   | <a href="#">LINK</a> |
|                                | Guideline on randomised controlled trials using real-world data to support regulatory decisions  | <a href="#">LINK</a> |
| <b>SFDA, Saudi Arabia</b>      | Real-world data in Saudi Arabia: Current situation and challenges for regulatory decision-making   | <a href="#">LINK</a> |
| <b>Swissmedic, Switzerland</b> | Swissmedic, Switzerland position paper on the use of real world evidence   | <a href="#">LINK</a> |
| <b>HSA, Singapore</b>          | Digital Health - UNDERSTANDING DIGITAL HEALTH PRODUCTS AND THE REGULATIONS   | <a href="#">LINK</a> |
| <b>NMPA, China</b>             | Guidance for Real-World Data Used to Generate Real-World Evidences   | <a href="#">LINK</a> |
|                                | Guidance on the Use of Real-World Evidence to Support Drug Development and Regulatory Decisions  |                      |
|                                | Guidance on Communication with Regulatory Agency on Real-World Studies to Support Product Registration   |                      |
|                                | Guidance on the Design and Protocol Development of Real-World Studies  |                      |
| <b>DKMA</b>                    | Danish Health data and registers   | <a href="#">LINK</a> |

| Jurisdictions                          | Regulatory Initiatives and Guidances  | Links   |
|--|---|---|
| <b>MHLW/PMDA,<br/>Japan</b>            | <p>Working group to deal with regulatory issues related to RWD:</p> <ul style="list-style-type: none"> <li>• Basic Principles on Utilization of Registry for Applications</li> <li>• Basic principles for utilization of medical information databases in post-marketing pharmacovigilance</li> <li>• Points to consider for Ensuring the Reliability in Utilization of Registry Data for Applications</li> <li>• Guidelines for the Conduct of Pharmacoepidemiological Studies in Drug Safety Assessment with Medical Information Databases</li> </ul>   | <a href="#">LINK</a>                                    |
| <b>MFDS,<br/>Republic of<br/>Korea</b> | <p>Guideline on the use of Medical Information Database (Real World Data) in pharmacoepidemiologic study</p>  | <a href="#">LINK</a>                                    |
| <b>Worldwide</b>                       | <p>ICH guidelines:</p> <ul style="list-style-type: none"> <li>• ICH M14 “<i>General principles on planning and designing pharmacoepidemiological studies that utilize real-world data for safety assessment of a medicine</i>”</li> <li>• ICH M11 “<i>Clinical electronic Structured Harmonised Protocol (CeSHarP)</i>”</li> <li>• ICH E6(R3) “<i>Good Clinical Practice (GCP)</i>” and Annex II on the use of RWD</li> <li>• ICH E8 “<i>General Considerations for Clinical Studies</i>”</li> <li>• ICH E9 (R1) (addendum on estimands) “<i>Statistical Principles for Clinical Trials</i>”</li> <li>• ICH E10 “<i>Choice of Control Group and Related Issues in Clinical Trials</i>”</li> <li>• ICH E11A “<i>Paediatric Extrapolation</i>”</li> </ul> <p>ISPE/ISPOR initiatives (non-exhaustive list):</p> <ul style="list-style-type: none"> <li>• HARPER (<a href="https://onlinelibrary.wiley.com/doi/10.1002/pds.5507">https://onlinelibrary.wiley.com/doi/10.1002/pds.5507</a>)</li> <li>• EQUATOR (<a href="https://www.equator-network.org/">https://www.equator-network.org/</a>)</li> <li>• ISPE guidelines for good pharmacoepidemiology practices (<a href="https://www.pharmacoepi.org/resources/policies/guidelines-08027/">https://www.pharmacoepi.org/resources/policies/guidelines-08027/</a>)</li> <li>• CIOMS Working Group XIII – Real World Data and Real World Evidence In Regulatory Decision Making</li> </ul> | <p><a href="#">ICH</a></p> <p><a href="#">CIOMS</a></p> |

## 162 Bibliography

- 163 Angelis, A., Lange, A. & Kanavos, P. Using health technology assessment to assess the value of new  
164 medicines: results of a systematic review and expert consultation across eight European countries. Eur  
165 J Health Econ 19, 123–152 (2018).
- 166 Bakker E, Plueschke K, Jonker CJ, Kurz X, Starokozhko V, Mol PGM. Contribution of real-world  
167 evidence in EMA regulatory decision making. Clin Pharmacol Ther. 2022 Oct 17. doi:  
168 10.1002/cpt.2766.
- 169 Cave A, Kurz X, Arlett P. Real-World Data for Regulatory Decision Making: Challenges and Possible  
170 Solutions for Europe. Clin Pharmacol Ther. 2019 Jul;106(1):36-39.



- 171 Concato, J, Stein, P, Dal Pan, GJ, Ball, R, Corrigan-Curay, J. Randomized, observational,  
172 interventional, and real-world—What's in a name? *Pharmacoepidemiol Drug Saf.* 2020; 29: 1514–  
173 1517. <https://doi.org/10.1002/pds.5123>
- 174 Concato J, Corrigan-Curay J. Real-World Evidence - Where Are We Now? *N Engl J Med.* 2022 May  
175 5;386(18):1680-1682.
- 176 European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP), 2022.  
177 ENCePP Guide on Methodological Standards in Pharmacoepidemiology, Chapter 15.6.3 ([link](#))
- 178 Flynn R, Plueschke K, Quinten C, Strassmann V, Duijnhoven RG, Gordillo-Marañon M, Rueckbeil  
179 M, Cohet C, Kurz X. Marketing Authorisation Applications Made to the European Medicines Agency  
180 in 2018-2019: What was the Contribution of Real-World Evidence? *Clin Pharmacol Ther.* 2022  
181 Jan;111(1):90-97.
- 182 Griesinger F, Cox O, Sammon C, Ramagopalan SV, Popat S. Health technology assessments and real-  
183 world evidence: tell us what you want, what you really, really want. *J Comp Eff Res.* 2022  
184 Apr;11(5):297-299.
- 185 International Coalition of Medicines Regulatory Authorities (ICMRA), 2022. ICMRA statement on  
186 international collaboration to enable real-world evidence (RWE) for regulatory decision-making ([link](#))
- 187 Jaksa A, Wu J, Jónsson P, Eichler HG, Vititoe S, Gatto NM. Organized structure of real-world  
188 evidence best practices: moving from fragmented recommendations to comprehensive guidance. *J*  
189 *Comp Eff Res.* 2021 Jun;10(9):711-731.
- 190 Jonker C, Bakker E, Kurz X, Plueschke K. *Front. Pharmacol.*, 04 August 2022, Sec. Drugs Outcomes  
191 Research and Policies
- 192 Kent S, Salcher-Konrad M, Boccia S, Bouvy JC, Waure C, Espin J, Facey K, Nguyen M, Rejon-  
193 Parrilla JC, Jonsson P. The use of nonrandomized evidence to estimate treatment effects in health  
194 technology assessment. *J Comp Eff Res.* 2021; 10(14):1035-1043.
- 195 Purpura CA, Garry EM, Honig N, Case A, Rassen JA. The Role of Real-World Evidence in FDA-  
196 Approved New Drug and Biologics License Applications. *Clin Pharmacol Ther.* 2022 Jan;111(1):135-  
197 144.
- 198 Eskola SM, Leufkens HGM, Bate A, De Bruin ML, Gardarsdottir H. Use of Real-World Data and  
199 Evidence in Drug Development of Medicinal Products Centrally Authorized in Europe in 2018-2019.  
200 *Clin Pharmacol Ther.* 2022 Jan;111(1):310-320.
- 201 Morton SC, Costlow MR, Graff JS, Dubois RW. Standards and guidelines for observational studies:  
202 quality is in the eye of the beholder. *J Clin Epidemiol.* 2016; 71:3-10.
- 203 RCT Duplicate publications: <https://www.rctduplicate.org/publications.html>
- 204 Simpson A, Ramagopalan SV. RWE ready for reimbursement? A round up of developments in real-  
205 world evidence relating to health technology assessment: part 4. *J Comp Eff Res.* 2022 Jan;11(1):11-  
206 12.
- 207 Simpson A, Ramagopalan SV. RWE ready for reimbursement? A round up of developments in real-  
208 world evidence relating to health technology assessment: part 8. *J Comp Eff Res.* 2022  
209 Sep;11(13):915-917.