# How to prepare for Policy 0070: Challenges and opportunities for clinical data publication in the EU


**John McIntyre, PhD**
Senior Consultant, Parexel Regulatory Strategy Consulting

**Ivan Tommasini, PhD**
Senior Director, Parexel Regulatory Strategy Consulting

**James Wolfe**
Vice President, Medical Writing Services, Parexel

**Simin Khaleeluzzama Takidar**
Senior Principal Medical Writer, Parexel

**Bipasha Das**
Associate Manager, Medical Writing Services, Parexel




parexel®

**Policy 0070 is a ground-breaking initiative and the European Medicines Agency (EMA) represents the first agency on a global level that will grant access to clinical trial data on such a large scale. With the requirements for all non-Covid products expected to restart in 2023, there is preparation required for qualifying submissions – which include new marketing authorization applications (MAAs) and clinical variations.**

The introduction of EMA's 'Policy 0070' in 2015 has heralded the publication of data from clinical studies in a publicly available database for anyone to scrutinise. The policy is part of EMA's commitment to data transparency and making data available for public scrutiny and future research, all of which are in the interests of public health [1]. Policy 0070 is being rolled out in two phases:

**Policy 0070 phase 1:** will publish so-called 'clinical reports' only. These are defined as clinical overviews and summaries, clinical study reports (CSRs), as well a limited number of CSR appendices (protocols/protocol amendments, sample case report forms, and documentation of statistical methods) that were submitted to the EMA as part of the centralized procedure for approval.

**Policy 0070 phase 2:** individual patient data (IPD) will be published. Prior to the rollout of Phase 2, EMA has committed to undertake a targeted consultation with relevant stakeholders. As this public consultation has not yet been initiated, Phase 2 of the policy is regarded as some way off at present.

At the outset, Policy 0070 was intended to apply to all medicinal products approved via a centralised procedure. In December 2018 however, EMA suspended the publication of clinical data as part of their business continuity plan related to Brexit preparedness and EMA relocation out of London. The policy remains suspended due to business continuity policy, further impacted by Covid-19. At the time of writing this article, only centrally approved Covid-19 therapies and Covid-19 vaccines require publication of their clinical data.

For the purposes of data publication under Policy 0070, sponsors can redact commercial confidential information (CCI) and must either redact or anonymise protected personal data (PPD). CCI refers to information not in the public domain and whose disclosure the sponsor considers may undermine their legitimate economic interest, for example details of a proprietary technology the company has invested significant resource to develop. PPD refers to information relating to an identified or identifiable natural person or so-called 'data subject', as defined by the GDPR [2]. This information, referred to as 'personal data', may include physical attributes, physiological factors, socioeconomic status, etc. that could be used directly or indirectly to identify an individual. Sponsors may elect to use either 'quantitative' or 'qualitative' approaches to assess the possibility of re-identification after anonymisation.

A qualitative approach is non-analytical in nature and qualifies/estimates the risk of re-identification using a qualitative scale (e.g., high, medium, low risk) based on the characteristics of the source data (e.g., location of trial sites, prevalence of the condition, trial sample size, etc), and a PPD redaction strategy is employed. A quantitative approach, in contrast, is analytical in nature and in essence provides a calculation of the probability of uniquely identifying an individual by quantifying the risk of re-identification of an individual person. In this approach, anonymisation strategies are applied to datasets, and redaction is limited to direct identifiers. Here a numerical threshold of acceptable risk should be set with a justification of this value. Sponsors should describe the risk before and after the application of the anonymisation process, in addition to stating whether the chosen threshold is 0.09 or lower (as recommended by the EMA [3] and the Institute of Management[4]). Regardless of which approach is taken, a threshold for risk of subject re-identification and justification of same should be set. EMA encourages sponsors to use quantitative approaches where possible, as they are based on empirical measurement and as a result are more precise, less subjective, and typically retain more data utility. During 2021 however, of 11 regulatory procedures published by EMA, only 1 used a quantitative approach to anonymise data in clinical reports [5].

The legal basis for the introduction of Policy 0070 by the EMA is Article 80 of Regulation (EC) No 726/2004. The scope of Policy 0070 includes clinical data submitted to the EMA after 1st January 2015 related to both marketing authorisation applications as well as 'Article 58' applications (medicines for use outside of the EU). It also applies to new indications or line extension applications submitted to EMA after 1st July 2015. When the business continuity measures which are currently in place are stood down, sponsors must therefore be ready to submit redaction packages for all ongoing and future centralised procedures/Art 58s, as well as deal with the backlog of data from 2015 onwards which will need to be submitted to EMA. To put the scale of the work for a single regulatory procedure in context, data from EMA's first annual report on Policy 0070 cited that 54 regulatory procedures resulted in publication of 1.3 million pages, i.e., over 24,000 pages per regulatory procedure [6].

The timeframe for the restart is unconfirmed, although EMA has indicated that 2023 will see the restart of the policy for new active substances, while legacy project timelines remain unclear [7].

Despite these challenges, Policy 0070 also provides hitherto unseen opportunities for biopharmaceutical and academic researchers aligned with EMA's objectives of the policy to avoid duplication in clinical trials, and allow for closer scrutiny and utilisation of clinical data. Heretofore, the results of clinical trials were mainly made available via publication of study results in peer-reviewed journals. Two of the key limitations with such publications relative to CSRs is (1) the brevity of data that are reported, with so-called 'compression factors' of up to 8000 fold [8], and (2) reporting bias (e.g., withholding negative results) [9]. Publication of clinical reports via Policy 0070 presents researchers with many opportunities including the conduct of novel analyses such as systematic reviews and meta-analyses; detailed analyses of safety profiles; data re-analyses; use of match-adjusted indirect comparisons where historical control data are required; easier derivation of margins and sample sizes in bioequivalence trials; and full disclosure of study protocols.

**Parexel's recent experience in submitting redaction packages to EMA underlines several important learnings for sponsors:**

- When creating a redaction package, sponsors should ascertain with the EMA the clinical reports that will be within scope of that redaction package together with timelines for these activities.
- Sponsors may even engage the EMA in a discussion of the proposed anonymisation strategy at a pre-submission meeting and can send them redacted samples for their feedback, allowing the sponsor to start with creation of a robust anonymisation report rooted in sound logic.
- The anonymisation report, ideally only one for a redaction package, should clearly describe and justify the anonymisation methodology employed, and outline how the approach chosen is deemed to adequately ensure that the chances of patient/personnel identification are minimal in that redaction package.
- For assessment of anonymisation, two options are available to establish if the data are anonymised:
    - One option relates to the anonymisation based on the fulfilment of three criteria (no possibility to single out an individual, no possibility to link records relating to an individual, and information cannot be inferred concerning an individual).

- The second option refers to the anonymisation based on the evaluation of the re-identification risk (the aim of the risk assessment is to determine how much de-identification/anonymisation is required in order to reduce the risk of re-identification to an acceptable level).

- The classification of direct and indirect identifiers and the associated anonymisation techniques, along with rationales or exceptions, as relevant to the submission is of particular importance in the anonymisation report. There could be a scenario where a second data controller (sponsor) is involved. However, there should be one anonymisation report included in the redaction package, with common approaches to be taken by sponsors for the anonymisation of variables.
- When considering what, if any, CCI may be redacted in the package, sponsors should refer to the rejection codes available in the external guidance [3] and create a justification table justifying the redaction of each CCI instance. It is noted that based on our experience, as well as a review of recently published data on the EMA clinical data website, the threshold for acceptance of what constitutes CCI is very high, and clinical reports typically contain minimal redaction related to CCI.
- Sponsors should consider preparing a list of roles (e.g., Intellectual Property (IP) Team, Publication Strategy Team) who can get involved in the CCI review/assessment process. In Parexel's experience, an automated tool supports efficient, predictable and consistent data anonymisation during the submission process.

## Policy 0070 and GDPR

Anonymisation of PPD is aligned with GDPR legislation, i.e., Regulation (EU) 2016/679. Yet alongside this is the requirement for 'data utility'. Although not fully defined in EMA's external guidance, it is loosely referred to as the 'usefulness of the data' in this guidance [3]. In Parexel's experience with EMA Policy 0070 redaction packages, more specific insight on the value of the utility of certain types of data in the clinical reports is gathered during draft review meetings where EMA regulatory reviewers discuss their comments on the redaction proposal. It is noted that a fuller definition for data utility has been proposed by The Organization for Economic Co-operation and Development (OECD) [10], which refers to the value of data as an analytical resource and comprises both the data's analytical completeness and analytical validity. While IPD disclosure under Phase 2 of Policy 0070 may be some way off, achieving the balance of data utility and anonymisation is predicted to be much more challenging given the nature of IPD.

Marketing authorisation holders should be aware of the potential fines that can be imposed under the GDPR resulting out of their Policy 0070 legal obligations. If a data breach were to occur, such a fine could be up to 4% of the annual company turnover or 20 million Euros – *whichever is greater*. A quick glance at Wikipedia shows us that the highest fine for any single company so far is 746 million euros (https://en.wikipedia.org/wiki/GDPR_fines_and_notices).

There is legal requirement under GDPR to protect an individuals' private data, **by design** (i.e., using built-in systems to ensure compliance) and **by default** (i.e., the minimisation of data collection, processing, and reporting). This means that marketing authorisation holders need to have predefined processes and systems to ensure that only necessary data are collected and processed, and data are anonymised appropriately.

The restart of clinical data publication under Policy 0070 is expected to commence soon. With this, sponsors will have to ramp up resources to work through their backlog and meet EMA submission deadlines. This will require agility and scalability, as well as a working knowledge of the process.

Parexel's team of data redaction and regulatory experts have a proven track record in the area. Contact us to discuss how we can guide you through these upcoming regulatory changes.

## References


1. European Medicines Agency policy on publication of clinical data for medicinal products for human use (2019). EMA/144064/2019. Published 21 March 2019. Available at: https://www.ema.europa.eu/en/documents/other/european-medicines-agency-policy-publication-clinical-data-medicinal-products-human-use_en.pdf
2. GDPR article 4. Available at: https://gdpr-info.eu/art-4-gdpr/. Last accessed 8th February 2023.
3. External guidance on the implementation of the European Medicines Agency policy on the publication of clinical data for medicinal products for human use (2018). EMA/90915/2016. Version 1.4 published 15 October 2018. Available at: https://www.ema.europa.eu/en/human-regulatory/marketing-authorisation/clinical-data-publication/support-industry/external-guidance-implementation-european-medicines-agency-policy-publication-clinical-data#current-effective-version-section
4. Sharing clinical trial data: Maximizing benefits, minimizing risk. Institute of Medicine (IOM). 2015. Washington, DC: The National Academies Press.
5. EMA annual report annex 23, 2021. Available at: https://www.ema.europa.eu/en/documents/annual-report/annexes-2021-annual-report-european-medicines-agency_en.pdf
6. EMA Clinical data publication (Policy 0070) report Oct 2016-Oct 2017. 2018. Available at: https://www.ema.europa.eu/en/documents/report/clinical-data-publication-policy-0070-report-oct-2016-oct-2017_en.pdf
7. EMA Management Board: highlights of December 2022 meeting. Available at: https://www.ema.europa.eu/en/news/ema-management-board-highlights-december-2022-meeting. Last accessed 24 January 2023.
8. Doshi P, Jefferson T. Clinical study reports of randomised controlled trials: an exploratory review of previously confidential industry reports. BMJ Open. 2013;3(2):e002496. Published 2013 Feb 26. doi:10.1136/bmjopen-2012-002496
9. Joober R, Schmitz N, Annable L, Boksa P. Publication bias: what are the challenges and can they be overcome?. J Psychiatry Neurosci. 2012;37(3):149-152. doi:10.1503/jpn.120065
10. OECD Glossary of Statistical Terms. Statistics Netherlands, Statistics Canada, Germany FSO, University of Manchester, 2005, Glossary of Statistical Disclosure Control, incorporated in paper presented at Joint UNECE/Eurostat work session on statistical data confidentiality, Geneva, 9-11 October 2005. Available at: https://stats.oecd.org/glossary/detail.asp?ID=6935 Last accessed 6th December 2022.

# With Heart™

We're always available for a conversation

Parexel International Corporation
2520 Meridian Pkwy, Durham, NC 27713, USA
+1 919 544-3170

Offices across Europe, Asia, and the Americas
**www.parexel.com**



parexel®