Regulatory Public Disclosure

SECTION EDITOR

Sam Hamilton
samhamiltonmwservices@gmail.com

doi: 10.56012/hnnl8161

Editorial

So far, activity in 2023 in the EU regulatory public disclosure (RPD) environment has been well-paced. By that, I mean that the regional and country agencies and sponsors are becoming more familiar with the Clinical Trial Regulation (CTR) and the Clinical Trials Information System (CTIS) space, and are knowledge- and information-sharing effectively enough to save stakeholders valuable time. The EMA information sessions and posted documentation are key resources that help sponsors with their clinical trial applications (CTAs) uploaded to CTIS. What we have not yet seen are the results emerging from the "back end" of CTIS, as studies conducted under the CTR remain active. As these studies begin to approach their end, this will surely herald another period of intense activity and learning for the community.

Recently, we have received notification that clinical data publication (CDP) for non-COVID indication studies will restart in Quarter 4 of 2023, so we will need to be prepared for both CDP relaunch under Policy 0070, as well as studies conducted under the CTR reporting through CTIS – which should be interesting – there will be differences. The Policy 0070 relaunch – or what we currently know of it – is nicely summarised below by Alison McIntosh. The public consultation to "Review transparency rules for CTIS" (https://www.ema.europa.eu/ en/news/review-transparency-rules-eu-clinical-trials-information-system-ctis) over the period May 3 to June 28, 2023, means that we can expect updates – and the outcome of an Accelerating Clinical Trials in the EU (ACT EU) public consultation (May to end June 2023) will drive the changes. We now have the July 10, 2023, "Guidance document on how to approach the protection of personal data (PD) and commercially confidential information (CCI) whilst using CTIS version 1.1" comprising chapters on personal data, commercially confidential information, and good clinical practice (GCP) inspection reports. All of this tells us that the authorities continue to "work it out", often with input from other stakeholders and end-users – and that none of this is simple! It is also wonderful to see inter-agency cooperation and dialogue ongoing through development of public disclosure-related guidances, with Health Canada and EMA working together on some initiatives.

The EU and Canada are not the only jurisdictions with a lively public disclosure landscape. Zuo Yen Lee, the CORE Reference Team's disclosure expert for Asia, shares relevant information for four key countries in Asia to help you navigate the authorities' requirements (p. 96).

So as a community at the sharp end preparing texts for public disclosure, hold your nerve and continue to keep yourself well-informed. The CORE Reference Special Project can support you with your learning (see box below).

Finally, you may be aware that EMWA's Regulatory Public Disclosure Special Interest Group (SIG) has been retired, and a broader-based SIG, the Regulatory SIG, is now up and running. The CORE Reference Team is to be a key contributor of RPD content for the new Regulatory SIG, and so our team hope to meet many of you at the SIG meetings.

Sam Hamilton
Chair, The CORE Reference Project

Clinical Data Publication (Policy 0070) relaunch

Alison McIntosh
aagmedicalwriting@gmail.com

doi: 10.56012/nnwx9514

In preparation for the relaunch of EMA Clinical Data Publication (Policy 0070), a webinar was held on May 16, 2023, and a video recording of the meeting can be viewed online (https://www.ema.europa.eu/en/events/clinical-data-publication-policy-0070-re-launch-ema-webinar).

EMA Policy 0070 relaunch applies to new active substances from September 2023 onwards and includes negative and withdrawn products. Invitation letters will be sent if your product is in scope. Notably, COVID-19 and other public health emergency clinical data publication continues. EMA has confirmed that pre-submission meetings specific to a product can be offered and encourages sponsors to make use of such meetings.

EMA recommends that Sponsors prepare their Policy 0070 packages early and prior to Opinion. A new Q&A document relevant to the 2023 relaunch of Policy 0070 has been developed by EMA to address a number of practical questions concerning procedural matters including timelines, commercially confidential information, and the anonymisation process.

In this Part 1 of the relaunch, there are no plans to request clinical data for products authorised during the suspension of Policy 0070. Step 2 of the Policy 0070 relaunch will look at the backlog of studies and may require some to be published, e.g., publication upon request for particular products.

Sponsors should review documents to make sure any proposed Commercially Confidential

Information (CCI) is not already in the public domain. Given the EMA's COVID-19 experience of CCI, they are not expecting to see CCI in clinical documents for Policy 0070.

A new Anonymisation Report (AnR) template with structured fields has been developed jointly with Health Canada (HC) to allow "one report for joint EMA/HC packages". The use of structured fields in the AnR template is to provide content predictability, consistency, and efficient writing.

A full quality control check prior to submission is to be completed by the Sponsor to confirm all necessary documentation is submitted. Based on EMA experience with COVID-19 clinical data publication, an updated cover letter includes a checklist to ensure validation success.

CORE Reference Special Project – Continual Professional Development

The EMWA Webinar titled "CORE Reference – Value for the Global Regulatory MW Community" was held on June 21, 2023. Topics included:

- Website (www.core-reference.org) and resources
- Practical utility of CORE Reference, including PDF open-book demonstration
- Transparency and disclosure in Asia
- EMA Policy 0070 relaunch 2023
- Q&A

The webinar recording, transcript of the chat, and PDF of the slides are available here: https://emwa.org/education/public-webinars/. Please share these resources widely in your professional communities.

Receive Continual Professional Development resources direct to your inbox (sign up at: https://www.core-reference.org/subscribe), or periodically check the News Summary page of the existing website (https://www.core-reference.org/news-summaries/) where information gathered on matters concerning RPD and clinical study reporting is archived monthly. A recent selection of the most relevant information in the world of RPD is in Table 1.

Table 1. Selected regulatory information shared via CORE reference (March 2023 – July 2023)

Disseminated information	Brief description	Link
March 2023 highlights		
CTIS training materials – Latest updates	EMA guidance document to help users to easily identify which are the latest updated materials on the EMA website and which materials have been developed since the last time users have consulted them.	https://www.ema.europa.eu/en/documents/other/ctis-training-materials-latest-updates_en.pdf
Clinical Trials Coordination Group (CTCG)	Q&A document to support sponsors submitting or transitioning their complex trials to CTIS.	https://www.hma.eu/fileadmin/dateien/HMA_joint/00-_About_HMA/03-Working_Groups/CTCG/2023_03_CTCG_QA_complex_clinical_trials_and_CTIS_v1.0.pdf
New UK law will require all drug clinical trials to rapidly report results: TranspariMED article	The UK government will introduce a legal requirement to make public the results of all drug clinical trials within 12 months of trial completion. The new law will also make it mandatory to pre-register trials and to share their outcomes with participants.	https://www.transparimed.org/single-post/uk-clinical-trial-law
Electronic systems, electronic records, and electronic signatures in clinical investigations: Q&A. FDA draft guidance	Provides information for sponsors, clinical investigators, institutional review boards, contract research organisations, and other interested parties on the use of electronic systems, electronic records, and electronic signatures in clinical investigations of foods, medical products, tobacco products, and new animal drugs under FDA regulations and revises the draft guidance for industry issued in June 2017 entitled *Use of electronic records and electronic signatures in clinical Investigations under 21 CFR Part 11 — questions and answers* and, when finalised, will supersede the guidance for industry entitled Computerised systems used in clinical investigations (May 2007).	https://www.fda.gov/regulatory-information/search-fda-guidance-documents/electronic-systems-electronic-records-and-electronic-signatures-clinical-investigations-questions?utm_medium=email&utm_source=govdelivery
Registration of clinical trials and public disclosure of results: Health Canada draft guidance	To provide guidance to sponsors of Health Canada-authorised clinical trials to support the registration and public disclosure of results (reporting of results) using international registries. Additionally, this document describes the clinical trial information that Health Canada is publishing on the Health Canada Clinical Trials Portal.	https://www.canada.ca/en/health-canada/programs/consultation-registration-clinical-trials-public-disclosure-results-new-guidance-public-search-portal/overview.html
April 2023 Highlights		
EU CTR Implementation: PHUSE blog post	Summary of Year 1 of the regulation from a sponsor perspective, with a focus on transparency aspects.	https://phuse.s3.eu-central-1.amazonaws.com/Deliverables/Data+Transparency/EU+CTR+Blog+Update_Year+1.pdf
CTIS - Sponsor Handbook, v. 3.02	This version includes newly added information about multi-factor authorisation in CTIS, as well as links to CTIS bitesize talks.	https://www.ema.europa.eu/en/documents/other/clinical-trial-information-system-ctis-sponsor-handbook_en.pdf
Diversity Plans: FDA Draft Guidance	The FDA recommends that sponsors develop and submit a diversity plan to help ensure the adequate participation of relevant and underrepresented populations and analyses of data collected from clinically relevant populations.	https://www.federalregister.gov/documents/2022/04/14/2022-07978/diversity-plans-to-improve-enrollment-of-participants-from-underrepresented-racial-and-ethnic
Considerations on evidence from single-arm trials: EMA reflection paper	The paper discusses key concepts for single-arm clinical trials that are submitted as pivotal evidence in support of marketing authorisation applications for medicines in the EU. Stakeholders are invited to send their comments via an online form by midnight (CET) on September 30, 2023.	https://www.ema.europa.eu/en/documents/scientific-guideline/reflection-paper-establishing-efficacy-based-single-arm-trials-submitted-pivotal-evidence-marketing_en.pdf

Disseminated information	Brief description	Link
Software and Artificial Intelligence (AI) as a Medical Device (SaMD and AIaMD, respectively): MHRA guidance	This guidance provides access to important Software Group outputs that might be of assistance. Software Group are responsible for taking all reasonable steps to assure the safety of SaMD and ensure the UK public have access to technology that meets a clinical need. They work across the MHRA to achieve this aim for SaMD and AIaMD.	https://www.gov.uk/government/publications/software-and-artificial-intelligence-ai-as-a-medical-device/software-and-artificial-intelligence-ai-as-a-medical-device
May 2023 highlights		
ICH Harmonised Guideline, GCP E6(R3)	This version of E6 includes an updated version of the already-released GCP principles and the protocol content has moved from Section 6 in E6(R2) to Appendix B in E6(R3).	https://database.ich.org/sites/default/files/ICH_E6%28R3%29_DraftGuideline_2023_0519.pdf
MHRA Inspectorate Blog: ICH E6(R3) GCP guidance - Step 2 Public Consultation	MHRA wishes to consult directly with UK stakeholders to compile and coordinate their comments to the ICH Expert Working Group.	https://mhrainspectorate.blog.gov.uk/2023/05/02/ich-e6r3-good-clinical-practice-guidance-step-2-public-consultation/
FDA discussion paper: Artificial Intelligence and Machine Learning (AI/ML) for drug development	This paper aims to communicate with a range of stakeholders and to explore relevant considerations for the use of AI/ML in the development of drugs and biological products.	https://www.fda.gov/science-research/science-and-research-special-topics/artificial-intelligence-and-machine-learning-aiml-drug-development?utm_medium=email&utm_source=govdelivery
Discussions for the next revision of the Declaration of Helsinki (DoH): Meetings for the WMA and IFAPP (The Global Newsletter on Pharmaceutical Medicine)	The WMA is committed to reviewing the DoH every 10 years and 2023 is the 10th year since the previous update (2013, Brazil). Discussions are ongoing with the aim to adopt the revised version at the General Assembly in Helsinki, Finland in October 2024. You can read more in the 34th issue of the IFAPP Newsletter starting on page 8.	https://ifapp.org/static/uploads/2023/05/IFAPP-TODAY-34-2023.pdf
EC guidance on the content and structure of the summary of the clinical investigation report	"This guidance aims to ensure that the summary of the clinical investigation report presents information about the design, conduct, analysis, and results of the clinical investigation in terms and in a format that are easily understandable to the intended user of the medical device." There is an equivalent requirement under the EU CTR – the Lay Summary of Clinical Study Results.	https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52023XC0508(01)
June 2023 highlights		
An overview of comments from the public consultation on the ICH M11 guideline, template, and technical specifications have been published.	These comments will be sent to the ICH M11 Expert Working Group for consideration in the context of Step 3 of the ICH process.	https://www.ema.europa.eu/en/documents/comments/overview-comments-received-ich-m11-guideline-clinical-study-protocol-template-technical_en.pdf, https://www.ema.europa.eu/en/documents/comments/overview-comments-received-ich-m11-template-step-2b_en.pdf, and https://www.ema.europa.eu/en/documents/comments/overview-comments-received-ich-m11-technical-specification-step-2b_en.pdf
Reminder to re-subscribe to receive the Clinical Trials Highlights Newsletter.	Issues from mid-July 2023 will only be circulated to re-subscribers.	https://ec.europa.eu/newsroom/ema/user-subscriptions/3201/create

Disseminated information	Brief description	Link
June 2023 highlights - continued		
EMA Virtual CTIS: Information Day on Oct 17, 2023, from 13:30- 17:30 Amsterdam time (CET)	The purpose of this information day is "to support sponsors of clinical trials in preparing and proceeding with the transition to meet the deadline of January 30, 2025". Commercial and non-commercial sponsors with experience in transitioning trials as well as representatives from EMA and EU/EEA member states will share insights and best practices. The registration for the event is through DIA Europe and it is a paid event. Ample time is foreseen for Q&A. Participants are invited to submit related questions by October 3, 2023 to emaevents@diaglobal.org	https://www.ema.europa.eu/en/events/clinical-trials-information-system-ctis-information-day
Modernised ClinicalTrials.gov	The modernised ClinicalTrials.gov is now available. To allow users time to adapt to the modernised website, the classic ClinicalTrials.gov website will remain available until it's retired in 2024.	https://www.clinicaltrials.gov/?utm_medium=email&utm_source=govdelivery and https://classic.clinicaltrials.gov/
July 2023 highlights		
ICH E6(R3) exploratory video	ICH has published a 9-minute video that provides the rationale for the update of GCP, and the foundational elements that the update aims to achieve.	database.ich.org/sites/default/files/ICH_E6%28R3%29_Guideline_GCP_Video_2023_0601.mp4
EMA CTIS webinar	The slide presentation from the "Clinical Trials Information System Webinar: Second Year of Transition" is available to view including Sponsor experiences and perspective on transitional trials.	https://www.ema.europa.eu/en/events/clinical-trials-information-system-webinar-second-year-transition#documents-section
Guidance document on how to approach the protection of personal data and commercially confidential information (CCI) while using the Clinical Trials Information System (CTIS). Version 1.1	A further update to the guidance which now includes Chapter 4 on CCI (Management of CCI in clinical trial information submitted to CTIS) and Chapter 5 (GCP inspection reports). Accompanying the guidance update there has been an update to Annex I (Acronyms) and Annex II is a template that applies to GCP inspections carried out to category 1 trials where the publication of clinical trial information is delayed by deferral.	https://www.ema.europa.eu/en/documents/other/guidance-document-how-approach-protection-personal-data-commercially-confidential-information-while_.pdf and https://www.ema.europa.eu/en/documents/template-form/annex-ii-guidance-document-how-approach-protection-personal-data-commercially-confidential_ir.pdf

Abbreviations: CFR, Code of Federal Regulations; CTIS, Clinical Trials Information System; EC, European Commission; GCP, Good Clinical Practice; ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use; MHRA, Medicines and Healthcare products Regulatory Agency; WMA, World Medical Association.

Keep up to date with Core Reference

Sign up to CORE Reference using this link: https://www.core-reference.org/subscribe to receive the regular, real time email updates in full, with current information on regulatory reporting and public disclosure which support the continuing professional development (CPD) needs of medical and regulatory writers. The topics covered in the more extensive email updates include FDA and EMA guidance and news, real-world data, transparency and disclosure resources and news, development strategy news, news from Asia, and regulatory guidances open for public consultation. The emailed information is collated monthly and archived here: https://www.core-reference.org/news-summaries/

Table 1 provides a selection of key information disseminated by the CORE Reference Project Team between March and July 2023. Thanks to Vivien Fagan (Vivien.Fagan@iqivia.com) for summarising.

Current clinical trial disclosure landscape in Asia

Zuo Yen Lee
Zuoyen.lee@gmail.com

doi: 10.56012/vxbm4667

The transparency and disclosure landscape in Asia has been rapidly evolving during the past decade. With respect to clinical trial registries, China launched its national registry, ChinaDrugTrials.org.cn, in 2013; South Korea introduced the new clinical trial disclosure platform through its Ministry of Food and Drug Safety (MFDS) in 2019; whilst Japan unified its three existing primary registries into a single clinical trial registry – Japan Registry of Clinical Trials (jRCT) – in 2020.

In Table 1, we provide an overview of the national clinical trial registries and the trial results disclosure practices for 4 Asian countries – China, Japan, South Korea, and Taiwan.

First, registration of all interventional clinical trials, with certain exceptions, in the national registries are required before subject enrollment in all four countries. Clinical trials can also be registered in a variety of other trial registries which may have been used long before these national registries, and which now serve as voluntary registries. Most of these voluntary registries are operated in both the local language and English, and are registered as a primary registry in the WHO International Clinical Trials Registry Platform (ICTRP) Network. Except for Taiwan, the clinical trial results should be posted on the registries within 1 year following study completion. The definition of "study completion" should normally be in the protocols of individual trials. We typically define the term as the date of the "last subject last visit" in the trial, but for trials with exceptionally long follow-up periods, it may be defined as the last visit of the treatment.

In China, trial results are posted on the ChinaDrugTrials.org.cn as a separate summary or overview document which, per the Center for Drug Evaluation (CDE) guidance, should at least contain the content of the clinical study report (CSR) synopsis as described in the ICH E3 guideline. The results summary is, however, not accessible to the public. In Japan and South Korea, on the other hand, trial results are posted within their registries in brief synoptic summaries, which mostly include the primary and key secondary endpoints, and these are accessible to the public.

For drugs that are granted marketing authorisation, the CDE in China also publishes the trial results in the format of CDE review reports and drug instruction manuals on the CDE website, whereas the Pharmaceuticals and Medical Devices Agency (PMDA) in Japan publishes certain sections of Modules 1 and 2 of the Common Technical Document, PMDA review reports, and data summaries of the drugs on the PMDA website. In all four countries, the disclosure of CSRs is not required by the regulation. Of note, all these countries follow the ICH E3 guideline for developing the CSRs, mostly with their own specific additional requirements.

Specifically for China, more background information on the existing voluntary clinical trial registries, the development of its current national registry, and regulations pertaining to drug registration in the country is presented in the Regulatory Matters section in this issue of *Medical Writing* on p. 98.

Table 1. Current clinical trial disclosure landscape in Asia – Trial registration and results disclosure

	 China	 Japan	 South Korea	 Taiwan
National clinical trial registry (mandatory)	Drug Clinical Trial Registration and Information Disclosure Platform http://www.chinadrugtrials.org.cn/index.html	Japan Registry of Clinical Trials (jRCT) https://jrct.niph.go.jp//	Ministry of Food and Drug Safety (MFDS) Registry https://nedrug.mfds.go.kr/searchClinic	Taiwan Clinical Trial Registry (TCTR) https://www1.cde.org.tw/ct_taiwan/
Type of trial	Interventional (including BE, PK, Phase 1-4) (Not required: Observational)	Interventional (Phase 1-4), Observational (Not required: BE)	Interventional (Phase 0-4) (Not required: Observational)	Interventional (Phase 1-4), Observational
Trial registration timeline	Before subject enrolment	Before subject enrolment	After the study obtains MFDS approval; before subject enrollment	After the study obtains TFDA/CDE approval; before subject enrollment
Results posting required	Yes	Yes	Yes	No

	China	Japan	South Korea	Taiwan
Results posting timeline	Within 12 months of study completion or before marketing authorisation (for trials supporting an NDA), whichever occurs first	Within 1 year of study completion	Within 1 year of "last subject last visit"	–
Public accessibility to posted results	No	Yes	Yes	–
Format of posted results	Uploaded as a separate summary or overview document. Per China CDE guidance, the results summary/ overview should at least consist of the content of the CSR Synopsis as described in the ICH E3.	Posted within the registry as brief synoptic summaries or summary in text boxes; limited trial results, mostly only include primary and key secondary endpoints. Posted as links to publications.	Posted within the registry as brief synoptic summaries or summary in text boxes; limited trial results, mostly only include primary and key secondary endpoints.	–
Language	Mandarin (Simplified)	Japanese, English	Korean	Mandarin (Traditional)
Other optional/ Voluntary registry	• Chinese Clinical Trial Registry (ChiCTR) • Centre for Clinical Research and Biostatistics – Clinical Trials Registry (CCRBCTR) • Acupuncture-Moxibustion Clinical Trial Registry (AMCTR) • International Traditional Medicine Clinical Trial Registry (ITMCTR)	–	Clinical Research Information Service (CRIS) (which may contain more comprehensive information than the MFDS registry)	ClinicalTrials.gov (many studies conducted in Taiwan are also registered on this registry where trial data may be provided via links to publications)
Other means of results disclosure (Type of document)	For approved drugs: CDE website (CDE review reports, drug instruction manual)	For approved drugs: PMDA website (Some sections of CTD Modules 1 and 2, PMDA review reports, summaries of data)	Not known	For approved drugs: TFDA website (Package insert)
CSR structure/Format	ICH E3 Specific requirements for the title page and appendices.	ICH E3 Separate comparison of Japanese vs. non-Japanese data is required (for Module 5.3.7).	ICH E3	ICH E3 For multinational trials, Taiwan safety and efficacy data summary should be included in the appendix.
CSR Disclosure	No	No	No	No

Abbreviations: BE, bioequivalence; CDE, Center for Drug Evaluation; CSR, clinical study report; CTD, Common Technical Document; MFDS, Ministry of Food and Drug Safety (Republic of Korea); NDA, new drug application; PK, pharmacokinetic; PMDA, Pharmaceuticals and Medical Devices Agency (Japan); TFDA, Taiwan Food and Drug Administration.

Note: The information in Table 2 is correct as of April 2023.