



CORE Reference: New guidelines of preparing clinical study reports for Japanese biopharmaceutical companies seeking international regulatory approvals

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Abstract



Background: As part of good submission practice, international regulatory authorities, academic organisations, and biopharmaceutical companies are preparing for public disclosure of clinical study reports (CSRs). Japanese companies seeking international regulatory approvals will need to prepare disclosure-ready CSRs. The International Conference for Harmonisation (ICH) E3 guidelines (1995) and the ICH E3 Q&A document (2012) were released before disclosure-ready CSRs were required. To address this gap, the new Clarity and Openness in Reporting: E3-based (CORE) guidelines¹ were published (2016). Although the Pharmaceuticals and Medical Devices Agency (PMDA) and the Japanese Pharmaceutical Manufacturers Association (JPMA) are founding members of ICH, we hypothesise that Japanese involvement in and awareness of the CORE guidelines are low.

Purpose: To investigate Japanese involvement in and awareness of the CORE guidelines.

Methods: To evaluate Japanese involvement, the open-access CORE publication was analysed for Japanese authors and reviewers. To evaluate Japanese awareness, social media related to the CORE publication was assessed and Japanese and English versions of the PMDA and JPMA websites were screened. Japanese and English versions of an online, 10-question, CORE awareness survey were developed, reviewed by Japanese and English CSR writers, and pilot tested with CSR writers from JPMA member companies (domestic and foreign).

Results: The CORE publication did not involve any Japanese authors or reviewers. International awareness of the CORE publication was evident (1,681 article accesses; Altmetric score of 32; 113 tweets from 24 users, as of 30 June 2016). The highest Twitter activity was from the US and Europe; there were no tweets from Japan. References to CORE were not found on the PMDA and JPMA websites. The pilot survey revealed low awareness about CORE among CSR writers in Japan (results from the final survey to a larger sample will be presented).

¹ Hamilton S. et al., Developing the Clarity and Openness in Reporting: E3-based (CORE) Reference user manual for creation of clinical study reports in the era of clinical trials transparency. Research Integrity and Peer Review. 2016 1:4 DOI: 10.1186/s41073-016-0009-4.

Background



- As part of good submission practice, international regulatory authorities, academic organisations, and biopharmaceutical companies are preparing for public disclosure of clinical study reports (CSRs).
- Japanese companies seeking international regulatory approvals will need to prepare disclosure-ready CSRs.
- The International Conference for Harmonisation (ICH) E3 guidelines (1995)¹ and the ICH E3 Q&A document (2012)² were released before disclosure-ready CSRs were required.

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- To address this gap, the new guideline “Clarity and Openness in Reporting: E3-based (CORE Reference) was developed.³
 - As Japanese involvement appeared to be limited during the preparation of the CORE Reference guideline, we hypothesised that awareness of CORE Reference would be low in Japan.
 - **Purpose:** To investigate awareness of CORE Reference in Japan.

What is CORE Reference?



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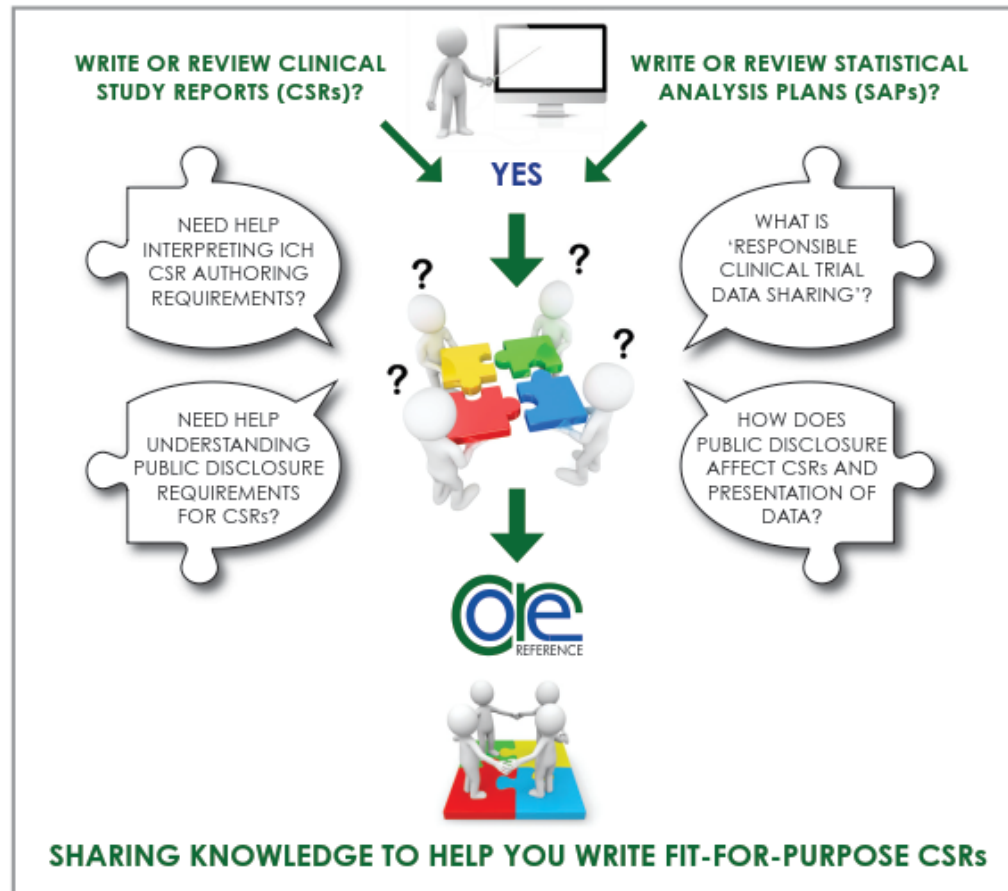
CORE Steering
Committee

<http://gappteam.org/about.html>



- **Clarity:**
 - CSRs must be clear, well-written, and free of ambiguity.
- **Openness:**
 - Health Authorities and the public require transparency, and public disclosure of clinical regulatory documents with CSRs being among the first for public disclosure.
- **Reporting E3-based:**
 - CSRs must serve the interests of regulatory reviewers by promoting reporting per ICH.

What is CORE Reference?



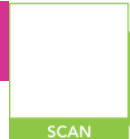
<http://www.core-reference.org/media/1039/core-leaflet-a4.pdf>

Methods

Social media research

- Social media related to the CORE publication (number of article accesses, Altmetric score, and number of tweets) was assessed.

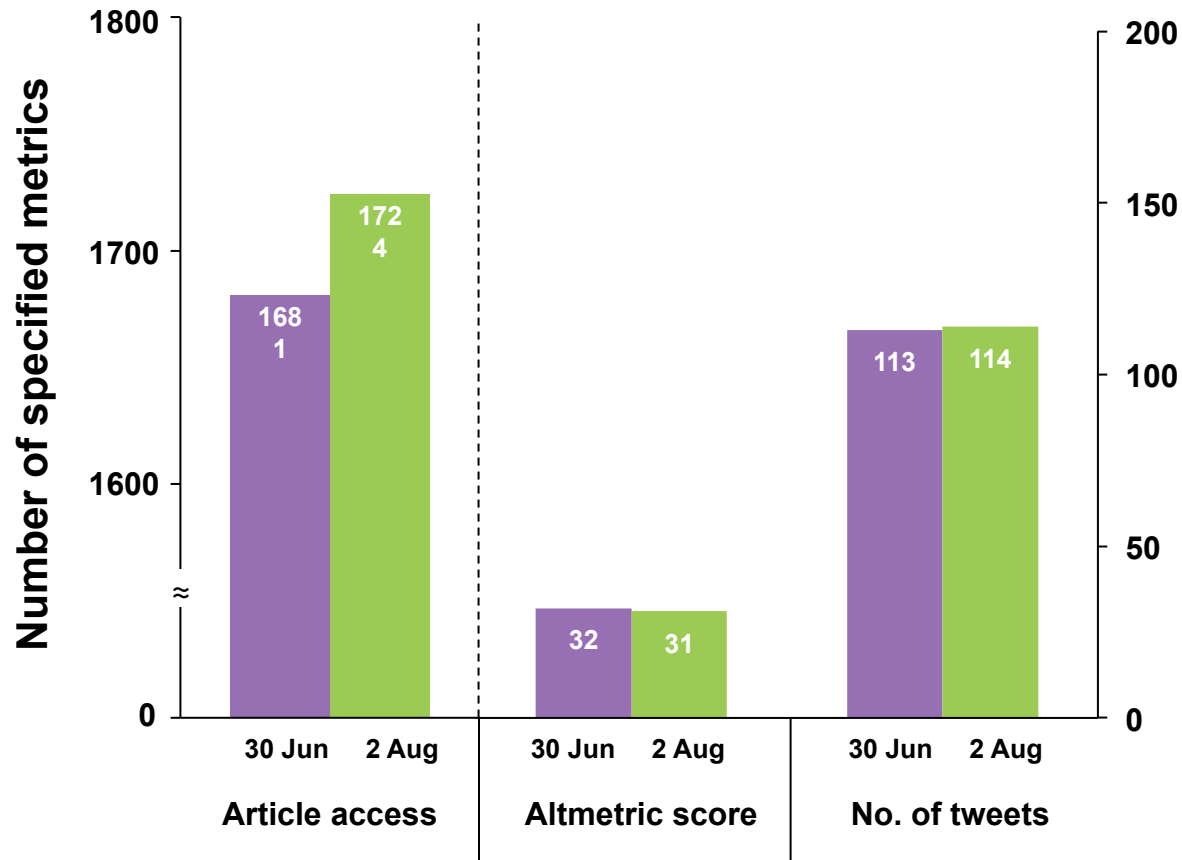
Questionnaire survey of JPMA pharma companies



- Survey target:
 - Medical writers or clinical representatives in charge of preparing CSRs and working for Japanese Pharmaceutical Manufacturers Association (JPMA) companies*.
 - * N=73 companies (as of 1 April 2016; JPMA website).
- Survey methods:
 - An online 10-question survey was administered via Survey Monkey®.
 - Request to complete the survey sent via e-mail (26 companies) and via mail (47 companies).
 - No financial incentives were offered.
 - An e-mail reminder was sent 3 working days before the end of the survey period.
- Survey period: From 19 July 2016 to 1 August 2016 (10 working days)

Results

Social media research



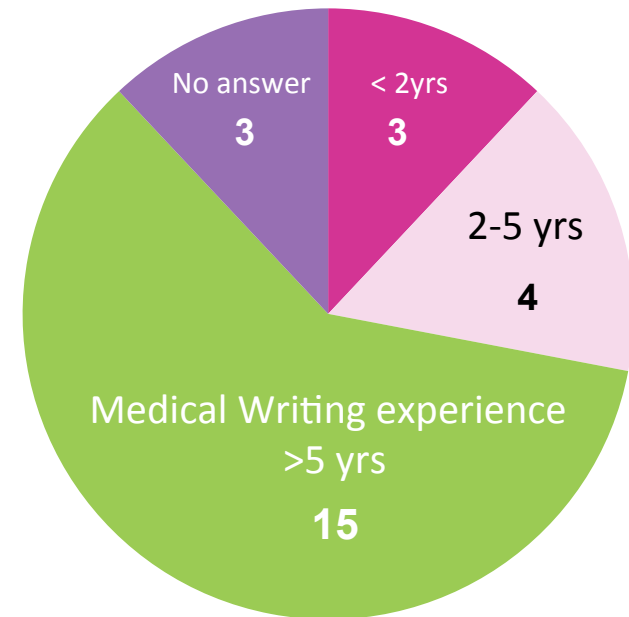
This research was done in 2016.

Article: <http://researchintegrityjournal.biomedcentral.com/articles/10.1186/s41073-016-0009-4>

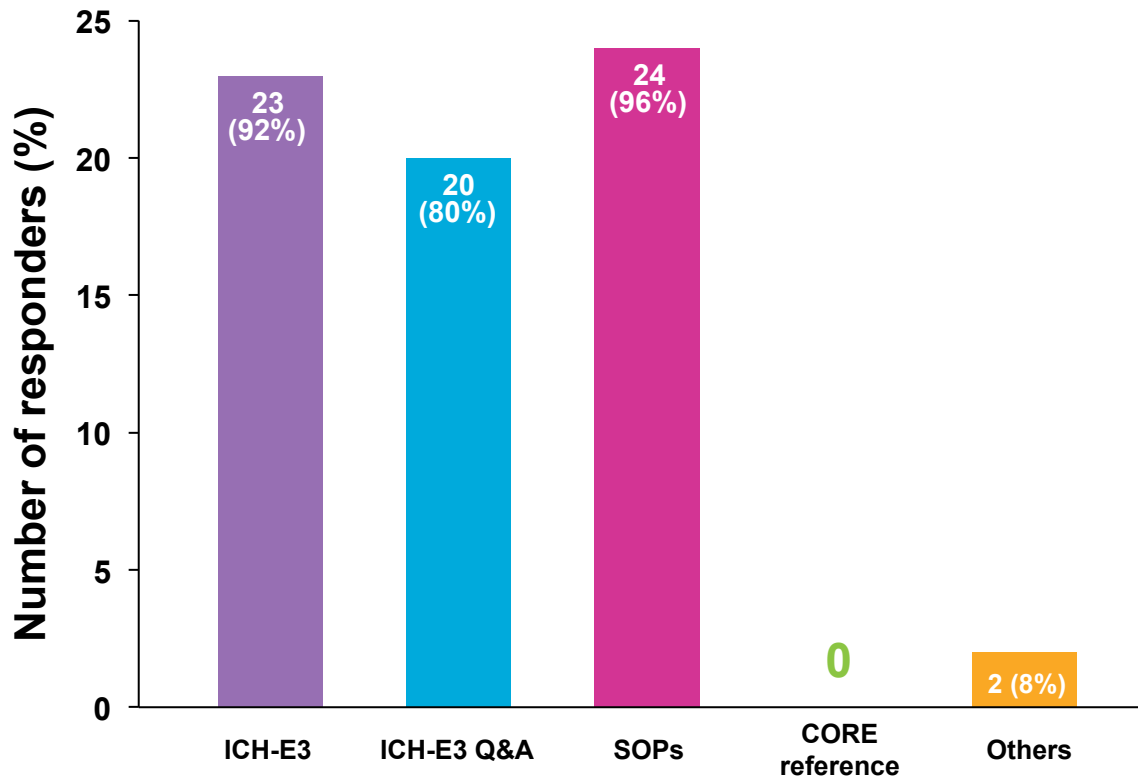
Altmetric It: <http://www.altmetric.com/bookmarklet.php>

Results

- Questionnaire survey of JPMA pharma companies
- 25 of the 73 JPMA pharmaceutical companies contacted completed the survey (response rate = 34%; 18 via website, 7 via mail).



- Guidelines used for preparing a CSR



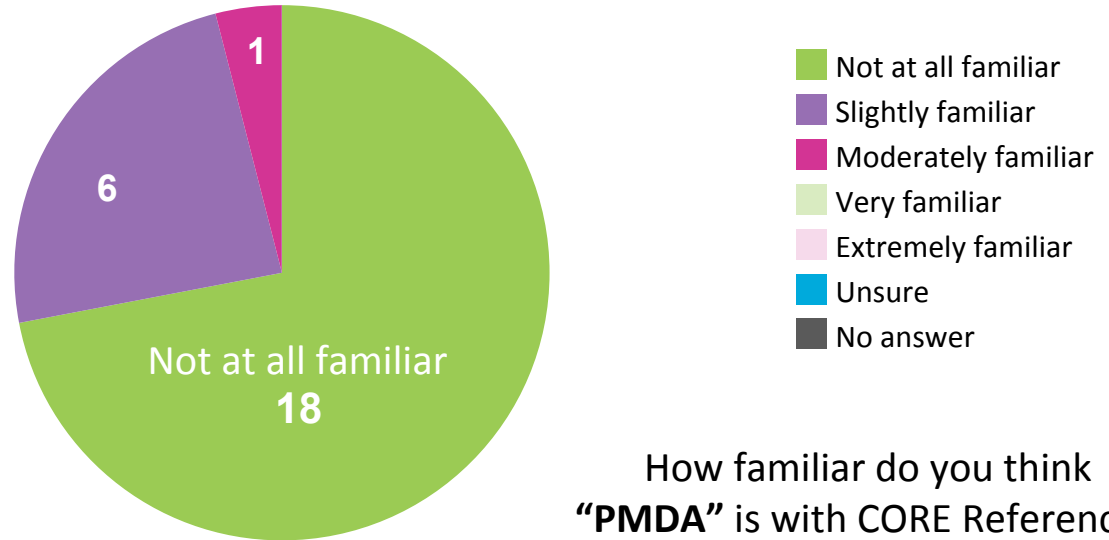
Multiple answers allowed, No answer 1,
Others: Yaku-shin No.335 (1 May 1996). ICH-E1, E9, E10, etc.

N=25 responding companies

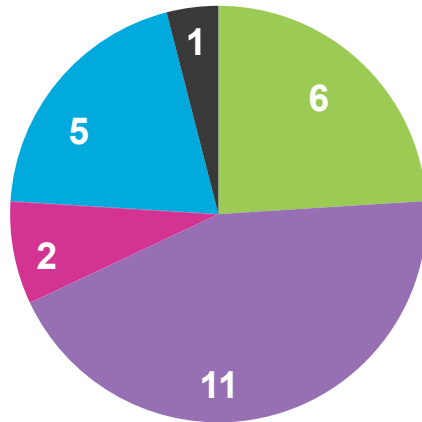


● Awareness of CORE Reference

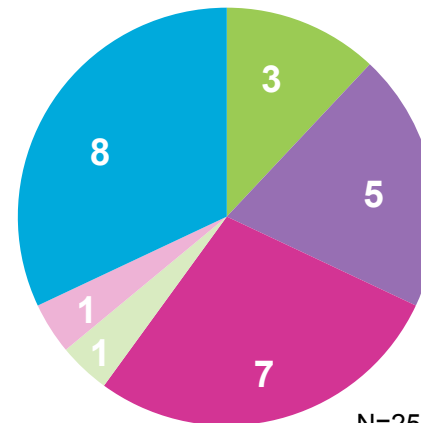
How familiar are “you” with CORE Reference?



How familiar do you think “Japanese medical writers” are with CORE Reference?



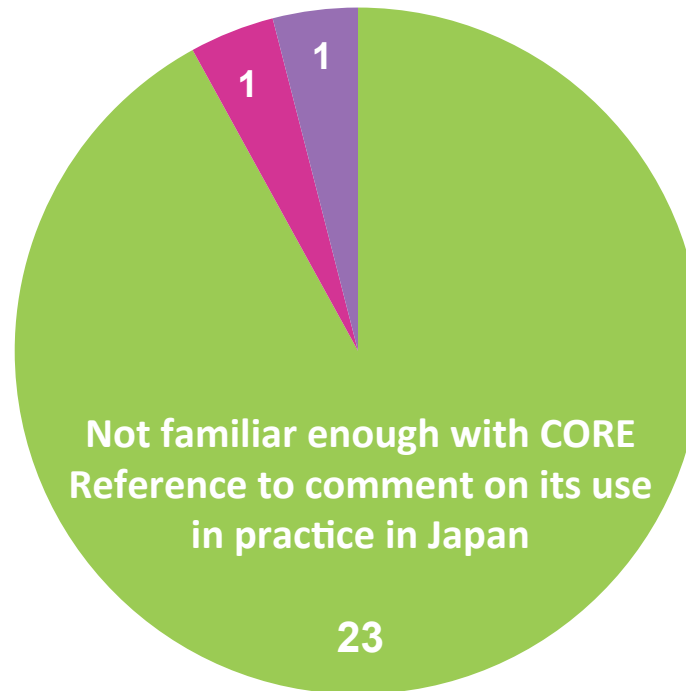
How familiar do you think “PMDA” is with CORE Reference?



- Impression of usefulness of CORE Reference

Familiar with CORE Reference AND believe it will be useful in practice in Japan

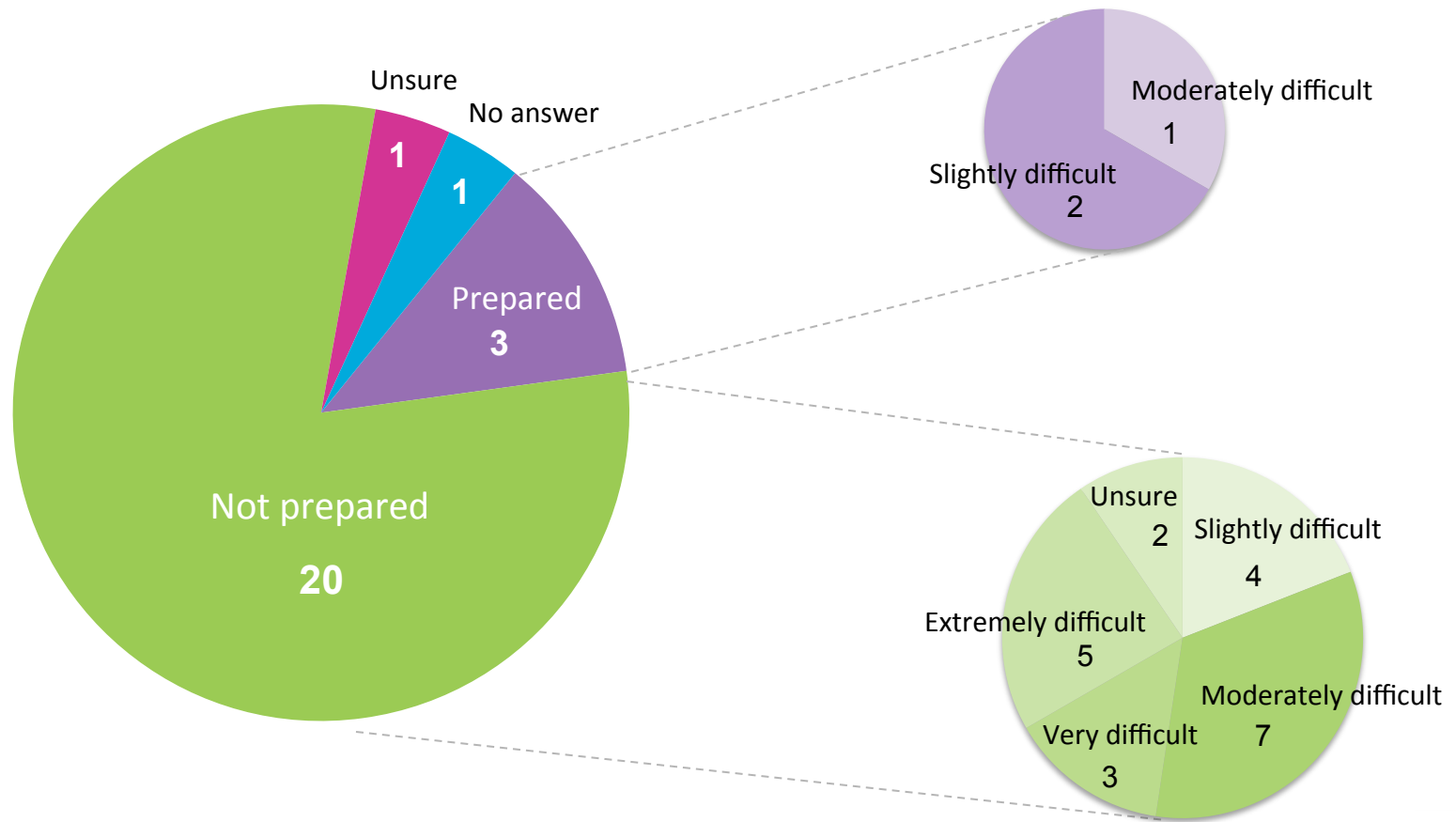
Familiar with CORE Reference, BUT don't believe it will be useful in practice in Japan



N=25 responding companies



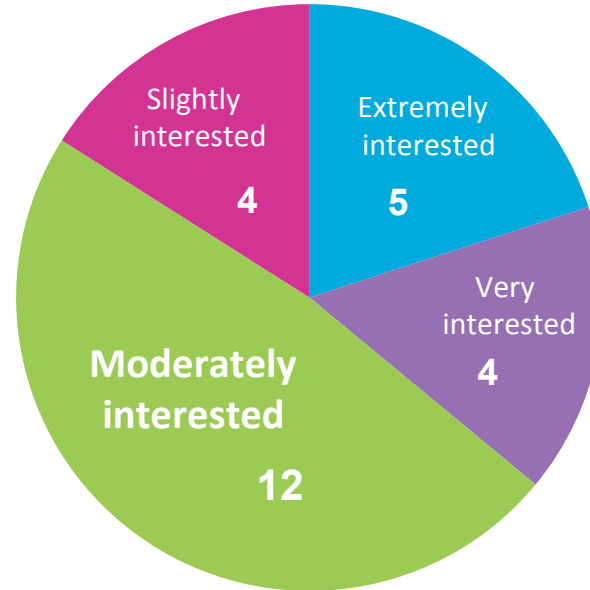
- Experience in preparing CSRs with redacted information and level of difficulty experienced or expected



N=25 responding companies



- How interested would you be in attending an educational seminar on CORE Reference?
-



N=25 responding companies



Limitations

- This analysis is based on answers from 25 of the 73 member companies of the JPMA. Answers from JPMA companies that did not respond or from non-JPMA companies may differ.

Conclusions

- Although awareness of CORE Reference may be increasing around the world, awareness of this new guideline is limited amongst those who prepare CSRs, whether working for Japanese or non-Japanese pharmaceutical companies.
- CORE Reference aims to enhance the timely, cost-effective, and low-risk preparation of ICH-compliant, disclosure-ready CSRs. Japanese companies seeking international regulatory approvals could benefit from education about CORE Reference.

References

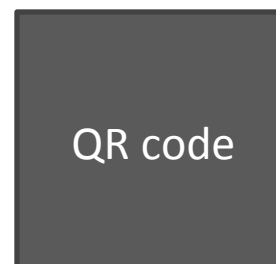
1. ICH Harmonised Tripartite Guideline: Structure and content of clinical study reports E3. Step 4. 1995.
http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E3/E3_Guideline.pdf.
Accessed 15 Aug 2016.
2. ICH E3 Guideline: Structure and content of clinical study reports questions & answers (R1). 2012.
http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E3/E3_QAs_R1_Step4.pdf.
Accessed 15 Aug 2016.
3. Clarity and Openness in Reporting: E3-based
<http://www.core-reference.org/> Accessed 15 Aug 2016.

Conflict of interest

- All authors participated in the research, were actively involved in preparing the abstract, and provided approval for submission.
- All authors are employees of the Envision Pharma Group and members of not-for-profit associations supporting ethical and effective medical writing practices.
- KW owns shares in Johnson & Johnson.

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- Graphic design support was provided by Evelyn Lee (Creative Solutions, ProScribe Pty Ltd, Part of the Envision Pharma Group).
- Please scan this QR code with your smartphone app to view an electronic version of this poster.
- If you do not have a smartphone, access the poster via the internet at <http:xxxxxxxxxxxxxxxx>.



English pptx version of the poster

Presented at the 6th General Meeting of the Society for
Regulatory Science of Medical Products.
September 9-10, 2016; Tokyo Japan (P-11)

[Questionnaire] Awareness and use of guidelines for preparing Clinical Study Reports

1. Do you work for:
 - A Japanese domestic healthcare company?
 - A Japanese affiliate of an international healthcare company?
 - Other (please specify _____)

2. How many years of medical writing experience do you have?
 - Fewer than 2 years
 - Between 2 and 5 years
 - More than 5 years

3. What guidelines does your company use to help prepare Clinical Study Reports? Please tick all that apply
 - ICH-E3 (1995)
 - ICH-E3 Q&A (2012)
 - Our company standards (eg, SOPs, templates)
 - Clarity and Openness in Reporting: E3-based (CORE) Reference user manual (2016)
 - Other (please specify _____)

4. International regulators are requiring public disclosure of Clinical Study Reports. Commercially confidential information and protected personal data can be redacted (masked/hidden). Have you or your Japanese colleagues prepared Clinical Study Reports with redacted information?
 - Yes
 - No
 - Unsure

5. How difficult do you think it is to prepare Clinical Study Reports with redacted (masked/hidden) information?
 - Not at all difficult
 - Slightly difficult
 - Moderately difficult
 - Very difficult
 - Extremely difficult
 - Unsure

6. How familiar are you with the CORE Reference User Manual? (<http://www.core-reference.org/>)
- Not at all familiar
 - Slightly familiar
 - Moderately familiar
 - Very familiar
 - Extremely familiar
7. How familiar do you think Japanese medical writers are with the CORE Reference User Manual?
- Not at all familiar
 - Slightly familiar
 - Moderately familiar
 - Very familiar
 - Extremely familiar
 - Unsure
8. How familiar do you think Japanese regulators are with the CORE Reference User Manual?
- Not at all familiar
 - Slightly familiar
 - Moderately familiar
 - Very familiar
 - Extremely familiar
 - Unsure
9. How interested would you be in attending an educational seminar on the CORE Reference User Manual?
- Not at all interested
 - Slightly interested
 - Moderately interested
 - Very interested
 - Extremely interested
10. In terms of your familiarity with the CORE Reference User Manual and its practical use in Japan:
- I am not familiar enough with the CORE Reference User Manual to comment on its practical use in Japan
 - I am familiar with the CORE Reference User Manual and believe it will be useful in practice in Japan
 - I am familiar with the CORE Reference User Manual, but don't believe it will be useful in practice in Japan



