SA01
EMA, Health Canada, FDA and PMDA: Four agencies tackle Data Sharing. Synergies and Differences

US Connect 2019, Baltimore
26. February 2019
Jean-Marc Ferran (Qualiance)
Jean-Marc Ferran leads the PhUSE Data Transparency Working Group since 2014 and represented PhUSE at the EMA Stakeholders Group meetings that took place during the development of Policy 0070 External Guidance. Jean-Marc joined later on the EMA Technical Anonymisation Group in 2017 and was a member of the Health Canada Stakeholders Group for Public Release of Clinical Data. Jean-Marc Ferran is also an Independent Consultant and supports d-Wise Technologies as an SME with the development of their Data Anonymization products.

The opinions in this presentation are my own.
• Brief Overview

• Comparisons of the 4 Initiatives
  – Processes
  – De-Identification Requirements

• In Practice
  – EMA Policy, 2 years on
  – Health Canada Draft Process
  – Focus on FDA approach
  – Insight into PMDA’s published documents

• To Discuss
  – Recognition Process?
  – Data Controllership?

• Conclusions
Brief Overview

Roundtables

Policy 0070 1st Draft

Policy 0070 Phase 1

Policy 0070 External Guidance

TAG

Industry Pilots

Policy 0070 Phase 1


ClinicalTrials.gov

gsk Roche efpiA

European Clinical Trials Database

EudracT

Health Canada White Paper

Health Canada Draft Guidance

Health Canada Draft Policy

Health Canada Stakeholders Group

Since 1999!
## Processes

<table>
<thead>
<tr>
<th>Item</th>
<th>EMA Policy 0070</th>
<th>Health Canada (Draft Guidance)</th>
<th>FDA (Pilot)</th>
<th>PMDA Disclosure of Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retrospective access to past CSR</td>
<td>Not in scope</td>
<td>In scope, based on prioritization system</td>
<td>Not in scope</td>
<td>Not in scope</td>
</tr>
<tr>
<td></td>
<td>Possibility through Policy 0043.</td>
<td></td>
<td>Possibility through FOIA request</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Sponsors conduct the redactions.</strong></td>
<td><strong>Sponsors conduct anonymization unless a certified EMA Policy 0070 document is available.</strong></td>
<td>FDA conduct the redactions</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Documents are sent to requester.</td>
<td><strong>Documents are made public.</strong></td>
<td>Documents are sent to requester.</td>
<td></td>
</tr>
<tr>
<td>Studies in Scope</td>
<td>All studies part of a Central Application <strong>regardless of submission outcome</strong></td>
<td>Step-wise approach over 4 years including Medical Devices studies from year 3 <strong>regardless of submission outcome</strong></td>
<td>Only Phase III pivotal studies <strong>CSRs following approval of an NDA</strong></td>
<td>CSR synopses included in Module 2 are in scope <strong>following approval</strong>, but full CSRs in Module 5 are out of scope</td>
</tr>
<tr>
<td>Recognition Process with other Agencies</td>
<td>None has been communicated so far</td>
<td>Yes with EMA through a certification application</td>
<td>Not discussed</td>
<td>None</td>
</tr>
<tr>
<td>Review Process (De-Identification of PPD)</td>
<td>Using Annotated Documents and Anonymisation Report. Comments and recommendation are provided.</td>
<td>Same as EMA but <strong>HC validates</strong> de-identification of patient information and keeps decisions on what is publicly released.</td>
<td>None but <strong>Sponsor can notify FDA of special-attention item in CSRs</strong></td>
<td>Sponsor states and substantiates rationale for redaction PMDA reviews and has final decision</td>
</tr>
</tbody>
</table>
## De-Identification Requirements

<table>
<thead>
<tr>
<th>Item</th>
<th>EMA Policy 0070</th>
<th>Health Canada (Draft Guidance)</th>
<th>FDA (Pilot)</th>
<th>PMDA Disclosure of Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Narratives in scope</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Mini-narratives for all SAEs in CSR synopses</td>
</tr>
<tr>
<td>Risk analysis</td>
<td>WP29 Opinion 3-Criteria Qualitative Qualitative</td>
<td>Quantitative only</td>
<td>“Qualitative” based on FDA’s approach for FOIA request</td>
<td>Qualitative – sponsor to justify all proposed redactions</td>
</tr>
<tr>
<td>De-Identification Technique</td>
<td>Anonymization &amp; Redaction</td>
<td>Anonymization</td>
<td>Redaction only based on FDA’s approach for FOIA request. In particular, “Demographic information, such as sex, age, and race, will generally not be redacted, except in very unusual circumstances”</td>
<td>Largely redaction with some transformations. PPD redaction is limited.</td>
</tr>
<tr>
<td>Guidance on Identification of Direct/Quasi Identifiers</td>
<td>Refer to PhUSE Standard and discuss in particular quasi identifiers such as: Dates Geographic Location Other Quasi-Identifiers (e.g. Demographics)</td>
<td>Indirectly-identifying variables are other identifying variables that fall within the definition of ‘personal information’ within Canada’s Privacy Act. And refer to Demographics and medical history and SAE. Country should remain unmodified.</td>
<td>Different type of identifiers discussed in Q&amp;A page: Unique Patient Identifiers Dates Clinical Trial Site Geographic Location Demographics Relative dates (study days) are retained</td>
<td>Redaction, with limited anonymization techniques e.g., rounding of age and generalization of dates</td>
</tr>
<tr>
<td>Guidance on Reference Population</td>
<td>No direct guidance but examples of plausible attacks to consider for risk modeling are listed.</td>
<td>4 populations are provided for consideration:   - Study Population   - Similar Sponsor Trials Population   - Similar Trials Population   - General Geographic Population</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>
EMA Policy 0070, 2 years on...

- 100+ Submission Packages published
- Sponsors still using in majoring qualitative approach coupled with redaction
- External Guidance updated 3 times, mainly for scope clarifications
- Due to Business Continuity Plan in connection with Brexit, Policy 0070 is posed since August 2018

Ref: Analysis of CSRs already published, PhUSE Review based on 47 submissions – Lukasz Kniola, November 2017
Health Canada Draft Process

Health Canada
- Final regulatory decision initiates proactive disclosure

Public
- Request from public initiates disclosure of past submissions

Health Canada
- Searches internal databases for submission and retrieves clinical information

Health Canada
- Sends clinical information to Manufacturer for processing

Has information been redacted for EMA?

Drugs only

Manufacturer
- Redaction of CBI
- De-identification of patient information

Health Canada
- Validates redaction of CBI
- Validates de-identification of patient information

Manufacturer submits certification of equivalency

Health Canada
- Uploads clinical information onto PRCI web portal
Focus on FDA Approach

- 1 Pilot Published so far, Janssen Pharmaceutica / ERLEADA
- Narratives out of scope, redaction only according to FOIA approach

Ref: “Drug Approval Package: ERLEADA” posted on FDA website, page 102, section 7.2.3.1 Deaths
• Dates such as Clinical Overview or Submission dates and study cut-off dates are considered CCI and can be redacted.

Ref: Gilead’s FTC/RPV/TAF FDC New Marketing Application Clinical Overviews published on PMDA website
Recognition Process?
Who is the Data Controller?
Sponsor or Agency?

• **EMA** provides recommendation and comments...

• **Health Canada** plans to validate de-identification of PPD...

• **PMDA** reviews and has final decision...

• **FDA** conducts the redactions and Sponsors can notify FDA of special-attention items in CSRs...
Conclusions

• **EMA and Health Canada initiatives are very similar** while FDA’s and PMDA’s differ significantly in anonymization requirements and processes
  – Will FDA consider anonymized CSRs already published in other jurisdictions when conducting redaction on same documents? And vice-versa?

• **Use of Study Days in the CSRs** could minimize the anonymization effort and seems accepted by all 4 agencies as anonymized dates

• The question of **Joint Controllership** should be clarified by all agencies as they review, validate or conduct anonymisation or redaction of documents

• **Four sources of same clinical documents** could be available in public domain. Which one will suit better the need of researchers?

• **Recognition processes** are only viable if there is an alignment of anonymization requirements
  – This will also allow for enhanced data utility and reduce risk of re-identification
Thanks!

Jean-Marc Ferran
Consultant & Owner, Qualiance ApS

dk.linkedin.com/in/jeanmarcferran/

@QualianceTwitta
## Engaging Stakeholders

<table>
<thead>
<tr>
<th>Item</th>
<th>EMA</th>
<th>Health Canada</th>
<th>FDA</th>
<th>PMDA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consultation on:</td>
<td>Policy &amp; Guidance through Stakeholders Review</td>
<td>Policy &amp; Guidance through Public Review</td>
<td>Planned “public feedback through a Federal Register notice and docket for public comments” following the conduct of the pilots</td>
<td>None</td>
</tr>
<tr>
<td>Pilot</td>
<td>None</td>
<td>None</td>
<td>9 pilots to be planned with sponsors</td>
<td>None</td>
</tr>
<tr>
<td>Working Groups</td>
<td>EMA TAG</td>
<td>Stakeholders Group</td>
<td>Not planned so far</td>
<td>NA</td>
</tr>
<tr>
<td>Working Groups Application</td>
<td>Public call for applications CV &amp; DoI required</td>
<td>Individual call for applications Application Letter &amp; DoI required</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Working Group Mandate</td>
<td>Maximum 2 years renewable</td>
<td>6 months between October 2017 and April 2018</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Working Groups Deliverables</td>
<td>Q&amp;A, Additional Guidance, Critical Review (TBA) developed by TAG members under EMA officers’ supervisions</td>
<td>Participation in 5 Meetings to comment on 5 key topics that led to the development of the guidance by Health Canada officers.</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>