The time for sharing of clinical trial data is not just approaching, it’s here. Beginning in January 2014, some members of Pharmaceutical Research and Manufacturers of America (PhRMA) and European Federation of Pharmaceutical Industries and Associations (efpia) launched the collaborative effort to allow researchers to request access to clinical trial data (clinicalstudydatarequest.com). The adoption of this industry driven attempt to make trial data available to independent researchers may help slow the proposed EMA regulations. No matter the solution approach, it is clear that public and regulatory body interest in trial data disclosure will not be going away.

Background
For the past few years, there has been growing public and regulatory calls for greater transparency into the drug development process. Reasons are mixed, but revolve around safety, efficacy, and outcomes. The regulatory response came from the European Medicines Agency (EMA) Policy 70, first published in June 2013. This policy, when approved, would require pharmaceutical companies to make anonymized (de-identified) trial data available for independent researchers for all those drugs submitted for marketing approval after the policy is in effect.

The industry response to the proposed regulations was issued in July 2013 as PhRMA and efpia “Principles for Responsible Clinical Trial Data Sharing”. These principles establish a guideline for sponsors to voluntarily self-regulate, and allows the sponsors some control of what study report data is made available to whom.

Current State
Momentum continues for more robust availability of trial data and for the implementation of the regulatory solution. Organized efforts like All Trials (AllTrials.net) keep this issue in the public eye, and garner support from medical and patient organizations. All Trial’s objectives are for disclosure of all trial data, past and present.

The PhRMA/EFPIA proposal started to be met in January 2014 by some companies that formed a voluntary consortium to develop and deploy clinicalstudydatarequest.com. This website has gone live and provides a mechanism for other companies to join. It does not meet the EMA Policy 70 approach in total, but works on a request basis with a review panel to review and approve/deny the request. It also provides access to SAS and R statistical programming on the site. Recently Novartis announced their intention to join this portal, joining five other companies.
So far, clinicalstudydatarequest.com has had 16 proposals for data submitted, and approved 12. None of the requests, at this time, have been rejected. This total does not include requests for data for studies that are not listed by sponsors on the website as available. This is an encouraging statistic, showing the interest level and success level of the requests.

There are also other models to follow for data sharing, such as Yale University’s Open Data Access (YODA) Project. This initiative started in 2011, and has been used by Medtronic which supplied the initial grant. Recently Johnson & Johnson (J&J) signed an agreement with the YODA project to make available trial data for new and existing drugs, as well as failed trials, a significant differentiation from other options. While this relationship will work for (J&J), the YODA project has not determined if they will broaden their scope to fill this role for other sponsors. Until the YODA Project data request portal is live, J&J has made Janssen R&D trials available via the website, clinicaltrialstudytransparency.com.

There are also software packages and service providers that specialize in meeting the current clinical trial disclosure requirements for clinicaltrials.gov. As for now, in the few that I have examined, there are no public statements of compliance to trial data transparency. The approach that makes sense for these vendors is to await definitive regulatory steps and work with an initial sponsor-as-partner to develop their process and/or solution.

On the regulatory front, Policy 70 is still in discussion for refinement and implementation. The expected discussion in mid-March was postponed recently with the next notification of progress and planning now due in June 2014. Since discussions continue both pro and con, there is some uncertainty what the final decision will be.

**Solution Decisions**

As a sponsor with plans to market a drug, and submission or approval looming, consideration will need to be made for the data from the development of the Clinical Study Report (CSR) to be made available publically.

- Who in the organization will be responsible?
  Data owners could be operational, e.g. Data Management, or therapeutic area aligned, maybe Compliance.
- What process will be in place for making the data available? There will be legal agreements to be developed and signed, review of requests, follow-up of the independent researchers.
- Where will the data come from? Clearly data collection from the trial and statistical analysis and results account for a large volume of data.
- How will the data be anonymized? Removal of patient identifiable information is key to public transparency.

**Why is independent review of trial data important?**

**Case study:** The UK Department of Health spent £424 million ($753 million) stockpiling the antiviral medication marketed as Tamiflu by Hoffmann-La Roche in case of an influenza pandemic.

A lack of consensus remains about how well the drug works, and there is disagreement about whether regulators received all available information on Tamiflu during the licensing process.

**Important:** With independent verification, payers can be certain that money is spent on efficacious treatments, an essential part of healthcare economics concerns.

**Source:** Canadian Medical Association [http://www.cmaj.ca/site/earlyreleases/13jan14_UK-parliament-calls-for-sharing-of-all-clinical-trial-data.xhtml](http://www.cmaj.ca/site/earlyreleases/13jan14_UK-parliament-calls-for-sharing-of-all-clinical-trial-data.xhtml)
People
Within the sponsor’s organization there are many roles that will be involved in the initial set up of this program. Some examples are:

- Data Management - extract the information used in the clinical study report
- Medical Director - guidance on data
- Legal - your company specific data request language; confidentiality, possible update to ICF language and HIPAA language
- IT - data consolidation, de-identification, transfer, security
- Compliance/Regulatory - track disclosed data usage
- Marketing - marketing may wish to know about the request and purpose
- Chief Medical Officer - same as marketing with no change to opt out
- Review Board – independent subject experts engaged for request review and approval (denial) purposes

Process
Some sample processes that need to be established are:

- Data collection or consolidation; data sources, cleaning, anonymization
- Request process; access, identification, submission, review, approval, denial
- Data access; access, download/transfer
- Tracking; requester research progress, results reporting, results data transparency

These processes do not have to be automated, especially if the volume of trials is low. Establishing these processes will enable the sponsor to be consistent in their transparency approach.

Technology
Certainly storing the collective clinical trial data is key to the ability to comply with transparency requests. Sponsors have some options in how this can be done, including developing a clinical data repository (CDR) or utilizing a package clinical platform like Oracle, Entimo, or SAS for example. Aside from the consolidation of the trial data, these repositories can serve additional benefits in the sponsor’s clinical development program by providing for additional analysis capabilities.

Making the data available is one step; access for independent researchers is another. Whatever portal is used needs to account for requests, board review and data dissemination. There will need to be some security and authentication set up. The above mentioned trial data access sites in the “Current State” section contain a similar approach.

DATA VOLUME

- 159,585 CLINICAL TRIALS
- 41,136 RECRUITING TRIALS

AVERAGE QUANTITY OF TRIAL DATA

- 11,074 CLINICAL TRIALS WITH RESULTS
- 11 PATIENT VISITS
- 13 ENDPOINTS
- 35 INCLUSION/EXCLUSION CRITERIA
- 167 PROCEDURES
- 169 CRF PAGES

Clarification for This Paper

Anonymized data will mean that all personal patient identifiable information will be removed with no ability to link backwards, per U.S. HIPAA regulations.

De-identification, not used in this paper but is used in EMA Policy 70 wording at the time of this writing, is the removal of personal patient identifiable information, with no link back, but can be interpreted to mean that there may be an expectation now or in the future of re-identification.
Risk-Based Approach

For companies looking to be prepared, there are sources mentioned above where the dialog can start, or they may look to work through some of the process on their own. The overall scope of the number of trials and volume of data can be overwhelming, but what companies can do is plan a strategy based on submission, approval and marketing plans.

To either meet the voluntary commitment or be prepared for Policy 70 approval, companies can reduce the volume of data to only those drugs with pending regulatory submissions or pending approvals. From the policy 70 standpoint, data availability will be required for the product to be marketed. If policy approval occurs in the next month to six months, companies should prepare the clinical data related to any product that is currently in the approval process or will be submitted in the next 12 months.

For some companies this “pilot” can reduce the volume of data, and workload to a manageable level to work through the process and technology needed to make the data available. It can also identify where problems, bottlenecks and other issues can occur thereby making any transition to larger volumes of data, easier as lessons learned are applied. This value-add can be timely should regulatory policy mandate a short time for compliance.

Next Steps

Collecting information and reporting it to government entities is not new to the industry. What is new is extent of the process and data management that must be done to ensure that the correct information is available for third parties. With our deep industry process and technology expertise, HighPoint Solutions has worked with our clients to leverage existing assets and combine the core components to meet many regulatory reporting requirements in the industry (e.g. aggregate spend, trial disclosure). Whether it is establishing your specific business processes, internal/external portal development, site security and hosting, data management and the workflow for electronic document review and approval, HighPoint can assist sponsors in meeting clinical data transparency needs.

It is clear that the regulatory and industry direction will overcome barriers of proprietary sponsor and patient information to move trial data transparency into a standard practice. It is important for sponsors to begin planning now, coordinate with key stakeholders and prepare how your company can meet these transparency initiatives, so that there is no interference with the submission, and launch of products that are the result of years of research and enabling companies to meet the therapeutic needs of their patients.

SOME RELATED EXPERIENCE:

• Online authoring, review, approval of regulatory submissions content
• Cloud centric data warehouse and analytics
• Clinical Data and Regulatory Affairs portal
• Multi-Sponsor Clinical Trial Portal
• Built and host Pharmaceutical Product Site Portals, internal and external