Meeting Minutes: Best practices for post approval changes workshop
3 of March 2021

Meeting recording can be accessed here:
https://www.dropbox.com/s/lwomyhbz66xldsm/Best%20practices%20for%20post%20approval%20changes%20workshop.mp4?dl=0

Key takeaways

1. **Collaboration** – proactive industry alignment (cross-modality and cross trade-trade associations) has made great progress during COVID-19 pandemic and demonstrates the potential to further improve communications.
2. **Convergence** – There is an urgent need to dramatically improve/ change the way we manage PACs among EMA, WHO and NRAs in order to provide and expand timely and equitable supply of vaccines to all populations, beyond borders.
3. **Clear guidelines** — clearly established international guidelines with broad adoptability will reduce complexity and provide clarity. WHO Annex 6 is a great example of a successful approach).

Resources provided in the meeting chat

- Alignment in post-approval changes (PAC) guidelines in emerging countries may increase timely access to vaccines: An illustrative assessment by manufacturers: https://www.sciencedirect.com/science/article/pii/S259013622030022X?via%3Dihub
- FDA Emergency Use Authorization for Vaccines to Prevent COVID-19: Guidance for Industry https://www.fda.gov/media/142749/download
- EMA Reflection paper on the regulatory requirements for vaccines intended to provide protection against variant strain(s) of SARS-CoV-2 https://www.ema.europa.eu/en/documents/scientific-guideline/reflection-paper-regulatory-requirements-vaccines-intended-provide-protection-against-variant_en.pdf

ITEM 1iii: [Q&A]

Post Approval Changes (PACs) – A Global Challenge - Thierry Gastineau, Sanofi

- To what extent will there be a need to conduct additional clinical trials with respect to PAC?
    - This is a great question and it depends on the type of change – so there is no single answer. Usually CMC changes with the ability to demonstrate comparability can avoid clinical trials but it is highly dependent on the type of change.

Case Study: Variation (PAC) Management for Vaccines- Parag Nagarkar, Serum Institute of India

- Can you address the role of inspections in gaining HA approval of the changes and any reliance that has been available or successfully applied?
    - This should be incorporated into the strategy - having a joint NRA with GMP inspection and capturing the aspects of supporting information helps WHO in securing a timely approval and various international approvals as well.
- Any thoughts on WHO review occurring concurrent with NRA review to reduce timing even further?
    - (Carmen Rodriguez Hernandez, WHO) - For Covid 19 vaccines, WHO PQ has established a global assessment mechanism of vaccines under EUL, which includes involvement of regulatory authorities in the review of rolling data and later facilitation of the outcomes of the review at global level. this is done in parallel to submission to NRAs as we cannot wait until the NRA of reference authorize to start reviewing aspects relevant to LMIC, that may not necessarily be considered by some authorities. For other vaccines, WHO has specific criteria published in the WHO PQ clearly stating under which situations we could accept parallel review.

Case Study: ERVEBO® (Ebola Zaire Vaccine) Streamlining Post Approval

- What are your thoughts on managing changes to a product that is sold in WHO dependent markets as well as other markets? For example, how would supply to Latin America countries be included in such an approach, e.g., single stockpile.
    - I am hopeful that we can collaborate with WHO-HQ and WHO's regional office (PAHO) to lead collaboration. There are current processes in place to allow this.
- We have been planning to submit the dossier in parallel to the reference NRA and WHO to facilitate a faster approval, but your recommendation seems to be to get NRA approval first, and then submit to WHO. Can you comment further on this - do you think parallel submission to the NRA and WHO does not actually speed up review/approval of a change?
    - If WHO-HQ agrees, an initial dossier could be submitted in parallel for initial registration, which is what we did for the Ebola Zaire Vaccine. My recommendation to gain approval of major post approval changes was for management of major post approval changes. You would still keep WHO informed that you were pursuing the major change, but you would not officially submit until you had approval. WHO can approve really quickly once all issues are resolved with the reference authority.

Case Study: COVID-19 vaccine – Diane Wilkinson, AstraZeneca

- How do your PACs relate to the SII and SK Bio versions of the AZ vaccine? Do they apply to these versions of the vaccine as well? Or will those versions have their own PACs?
    - It will depend - we are trying to share info across the companies we are working with.
- What are the challenges of AZ Covid vaccine manufactured in numerous sites across the world e.g., Alignment of Regulatory approval of countries where the vaccine is manufactured with EMA, need for bridging studies of AZ vaccine produced in these sites?
    - At this moment this has not been necessary, but we have seen very good robust comparability data from the manufacturing sites we are working with.

Industry Perspective – Andrew Deavin, GSK

- No discussion points noted.

Regulatory perspective – Carmen Rodriguez Hernandez, WHO

- No discussion points noted.

Meeting close and discussion

- A question to all speakers: please share your opinion regarding COVID-19 VOC and the need of additional clinical trial to access those variants X PACMP
    - Thierry: A major change to vaccines would constitute the need to gather additional clinical data. There is currently not a correlate of protection which means we are not in a similar situation to annual flu strain changes. There are a few papers that have been published suggesting immune bridging studies may be requested. On the PACMP's are for CMC changes which do not have a potential impact on the safety and efficacy – the purpose of this is to submit a protocol to downgrade the reporting of the change when you get the result of the protocol – perhaps this process could eb followed when CMC changes drive the need for clinical data
    - Carmen: WHO is working to address the issue of the variants and has developed the document on considerations for evaluation of COVID-19 vaccines and is preparing another iteration of that: https://www.who.int/publications/m/item/considerations-for-the-assessment-of-covid-19-vaccines-for-listing-by-who