VBI VACCINES

ACTIVATING THE POWER WITHIN

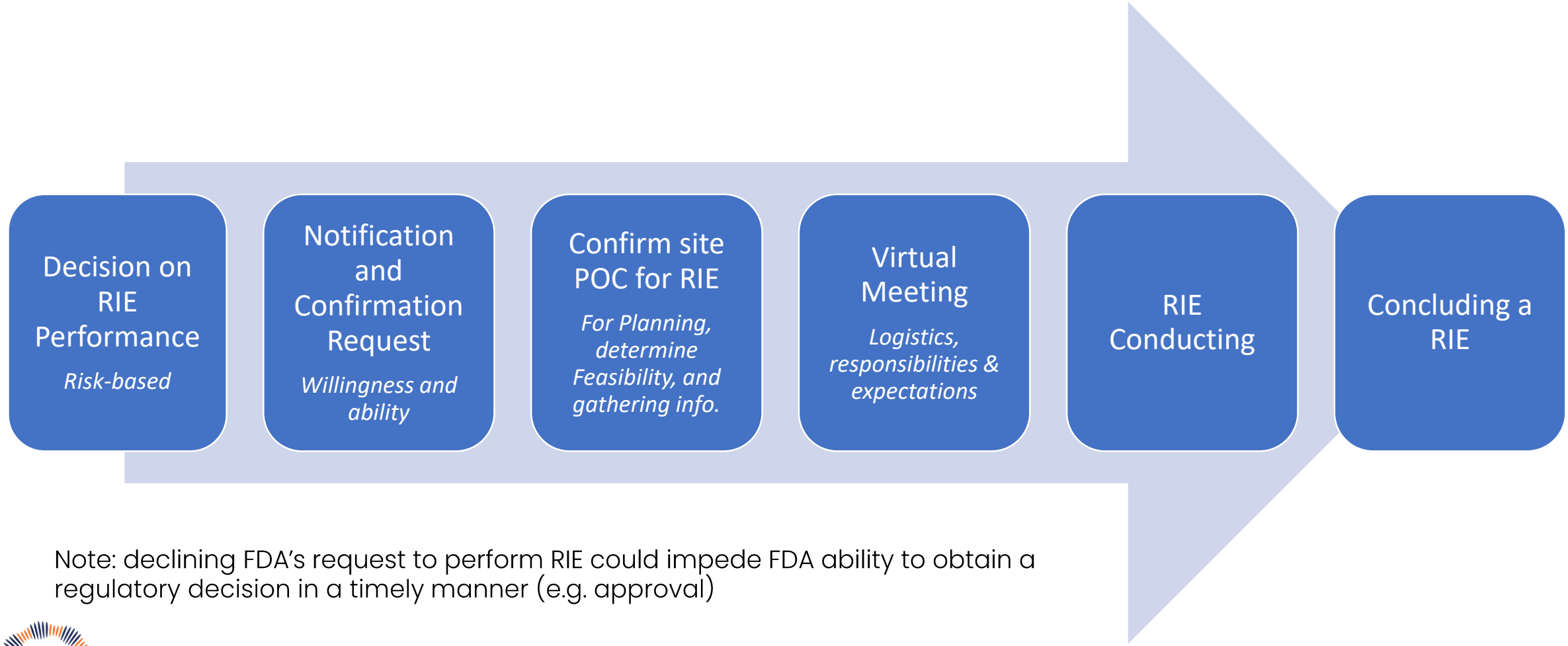
FDA Remote Interactive Evaluation

October 2021

Background: RIE – Guidance for Industry

- **Issued on April 2021** ("Remote Interactive Evaluations of Drug Manufacturing and Bioresearch Monitoring Facilities During the COVID-19 Public Health Emergency").
- Addressing the **COVID-19 public health emergency** – in effect only for the duration of public health emergency (declared by Secretary of Health and Human services).
- RIE- Interactive tools (/combination) to support regulatory decisions and oversight of facilities developed for cases that are not considered as mission-critical, are not a prioritized domestic inspection or are impacted by travel restrictions.
- **Includes various inspection programs** (Pre-Approval inspections, Post-Approval inspections, Surveillance and others). Conditioning: No DI or other issues that require an inspection, acceptable inspection history, may support assessing risks (application, manufacturing risks).
- May be also used to evaluate **defect reports (FAR, BPDR).**
- **Risk management** tools will be used to determine appropriate cases for RIE application.
- FDA does not accept request to perform RIE from applicants.

Background: RIE – Guidance for Industry



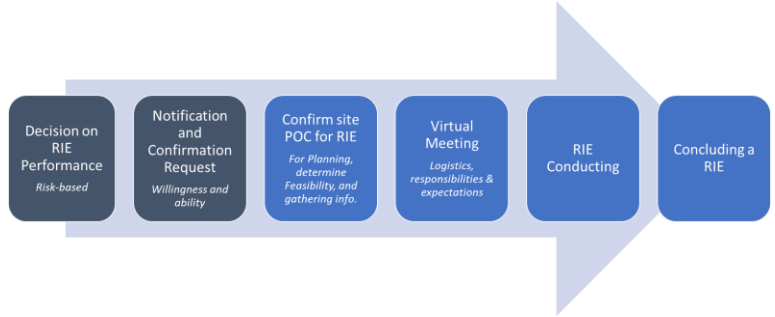
Note: declining FDA's request to perform RIE could impede FDA ability to obtain a regulatory decision in a timely manner (e.g. approval)

Background: VBI's application

- SciVac is a finished product manufacturer, manufacturing a third-generation Hepatitis B vaccine. The company is a subsidiary of VBI Vaccines Inc.
- Application for the drug product (marketed in IL under the commercial name "Sci-B-Vac 10mcg/ml) was submitted to FDA at the end of 2020. Expected finalization date of assessment: End of 2021.
- During 2019 SciVac has initiated an "Audit preparation program" which included several mock audits (consulting firms), official inspections , cooperation with consultants in specific fields (CSV, AP) etc.
- Intensive activity during 2021 – questions, clarifications, additional information required to be completed.

Decision On RIE Performance & Notification

- FDA approached SciVac with a list of requested records for evaluation (April 2021).
- Records associated with the quality, facility and equipment, materials management, production, labeling and packaging, laboratory systems.
- Last audit report by IMoH was requested for a review as well.
- A TC with FDA quality assessors with regards to manufacturing plans and travelling restrictions to IL.
- Meanwhile at SciVac- uncertainty.
- Final decision taken and communicated to SciVac during July 2021. SciVac was requested to voluntarily confirm its willingness and ability to participate in the in the RIE.
- RIE is performed by CBER for the first time.



Preparations at SciVac

Preparations for a remote audit started once the decision on RIE was communicated. 4 main channels:

- A. IT equipment & infrastructure
- WiFi and cellular coverage, upgrade of meeting rooms (cameras, dedicated laptops, audio streaming), Audio streaming during tour.
- B. Virtual Tour (Livestream video and recording)
- Recording of manufacturing stages in advance vs. livestream by dedicated equipment/Cell phone camera.
- C. Virtual Session management (Zoom)
- Camera, audio, Real-time documents sharing, screen sharing, Break Rooms management, video sharing (consultant), Internal zoom groups, mute.
- D. Staff (Working groups)
- Designated team for each auditor composed of: Host, Scriber, Back room responsible. Backroom manager. Emergency issues team.

Confirm POC for RIE & Virtual Meeting

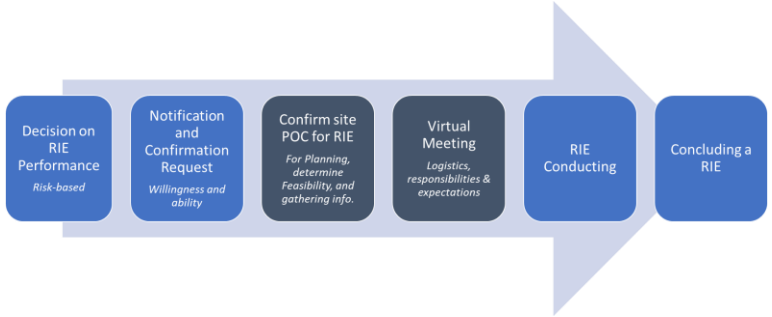
- At the time of RIE decision, RIE lead was chosen by the FDA. RIE leader approached the Quality Director of SciVac, who was confirmed as the RIE POC.
- Proactively contacting the RIE lead several times (email, telephone, TC).
- Prior to the virtual meeting a preliminary records request file was provided by lead auditor. 3 aspects:

(1) Inspection Logistics.

(2) Documents to be shared.

(3) Pre-recorded videos.

- **A virtual (feasibility)meeting** was scheduled several weeks prior to RIE date, with clear objectives (livestreaming quality, File sharing , virtual room management).
- In practice the meeting focused on the planned objectives with no professional discussions.
- Participation of auditors, department manager and IT person (FDA), QA personnel and IT person (SciVac).
- Building trust (transparency).
- Conclusion was shared with SciVac.



RIE Conducting

- **FDA form 482** (Notice of Inspection) was not issued as per applicable guidelines.
- Opening meeting with participation of global management and global quality representatives.
- With the exclusion of specific characteristics of remote interaction, **most of on-site audit principles are kept.**
- 6 days in total, 12:00-20:00 IL time.
- **Audit plan updates during the process.**
- Management of topics and SMEs.
- **Focused on topics that were requested to be shared** in advance, with requests for clarifications or additional data.
- **Consistent transparency and cooperation.**
- **Addressing concerns in real-time.**
- **Summary** of topics was frequently requested. Presented as presentation/flow chart.
- Materials presented were uploaded to the BOX as per auditors' request.
- **Summary meeting** at each day.

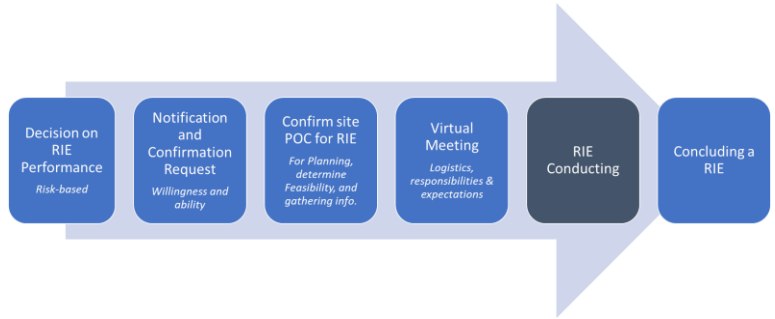
RIE Conducting (Tour & Simulations)

Live tour

- Connection to Zoom session with a cellular phone for livestreaming (two-way audio equipment).
- Scriber located in backroom is connected to Zoom session; Host responsible to follow up and verify appropriate streaming and sound.
- Consistent guidance & explanations.
- Performed in the order of the manufacturing process (DS>DP>Supporting systems).

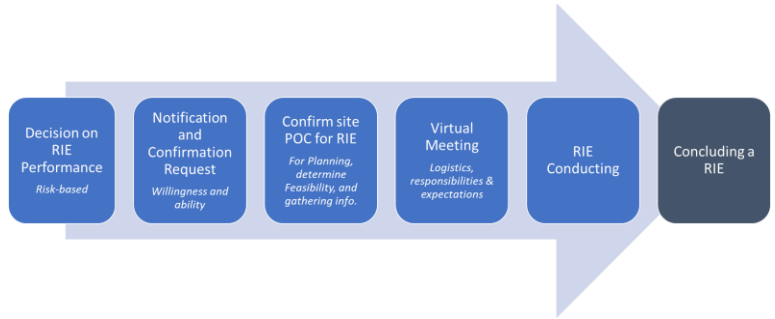
Real-time Simulations

- were requested following review of videos of the process.
- Livestreamed using tour cellphone/room cameras.
- Workstation next to streaming area.



Concluding a RIE

- Summary meeting of audit the end of last audit day with participation of global management and global quality representatives.
- Observations memo.
- As per applicable guidelines, FDA form 483 (Inspectional Observations) is not issued as part of RIE concluding.
- At SciVac- uncertainty.
- Response is expected in 15 U.S. business days.
- Following response, the lead auditor has provided the final RIE report.



Conclusions & Recommendations

- Preliminary connection with lead auditor
- Open discussion.
- Transparency.
- Initiative and proactivity.
- Addressing concerns in real-time.

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