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Report of the World Health Organization (WHO) Biosafety Inspection Team of the Variola Virus Maximum Containment Laboratories to the State Research Centre of Virology and Biotechnology ("SRC VB VECTOR"), Koltsovo, Novosibirsk Oblast, Russian Federation, 28 January- 2 February 2019

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Report from the World Health Organization Biosafety Inspection of the Variola Virus Maximum Containment Laboratories to the Federal Budgetary Research Institution - State Research Centre of Virology and Biotechnology "VECTOR" of the Federal Service for Surveillance on Consumer Rights Protection and Human Well-being (FBRI SRC VB "VECTOR", Rospotrebnadzor)

Koltsovo, Novosibirsk Region, Russian Federation
28 January–2 February 2019

EXECUTIVE SUMMARY

The World Health Organization (WHO) team of international experts carried out a biosafety and biosecurity inspection at one of the two WHO-authorized variola virus (causative agent of smallpox) repositories: VECTOR*, in January/February 2019 in accordance with World Health Assembly resolution WHA60.1 (2007). [*the Federal Budgetary Research Institution - State Research Centre of Virology and Biotechnology "VECTOR" of the Federal Service for Surveillance on Consumer Rights Protection and Human Wellbeing (FBRI SRC VB "VECTOR", Rospotrebnadzor)]

The activities of the WHO inspection team included inspection of the physical maximum containment facilities, the supporting engineering systems and the long-term secure specimen storage arrangement and the newly renovated isolation hospital. Before entry into the maximum containment facility, the inspection team performed a detailed review of the recent decontamination process. The inspection team had interactive discussions with VECTOR staff, requested and reviewed instruction manuals, standard operating procedures (SOPs) and other relevant biological risk management documents.

Management and staff at VECTOR described their institutional commitment to biosafety and biosecurity by delivering detailed presentations of their facility systems and operations throughout the inspection. The team presented and discussed with a representative of Rospotrebnadzor's Central Office and with VECTOR staff their findings of the inspection.

Since the last inspection in 2016, VECTOR has made significant improvements with many previous findings addressed and closed. The inspection team delivered a presentation at the end of the meeting related to the status of the various findings. The inspection team did not note any new findings

requiring immediate corrective actions (Priority 3) during the 2019 WHO inspection, although they have requested further work to improve some of the biosafety-related procedures pertaining to variola virus work.

In conclusion, the VECTOR repository was found to meet international levels of biosafety and biosecurity for variola virus research and storage. This inspection report places no responsibility on the WHO. Continued safe, secure storage and conduct of work with live variola virus remains the responsibility of VECTOR. The WHO requests VECTOR to submit an action plan to address the issues noted here for further improvement within 30 days of receiving this report.

CONTEXT

1. There are two authorized repositories of variola virus, namely, FBRI SRC VB "VECTOR", Rospotrebnadzor in Russian Federation and the Centers for Disease Control and Prevention (CDC) in the United States of America. The World Health Assembly resolution WHA60.1 (2007) requests that the WHO maintain inspections of the two laboratories biennially in order to ensure that the conditions of storage of variola virus and research conducted in the laboratories meet the highest requirements for biosafety and biosecurity. In addition, in accordance with resolution WHA60.1, inspection mission reports should be available for public information following appropriate scientific and security redaction.

2. Dates for inspection of both repositories are coordinated with annual maintenance of the facilities, following decontamination. This allows the inspectors to enter areas of the facilities that are difficult to access during the handling of live variola virus. The WHO inspection team, consisting of international experts in a range of fields, visited VECTOR from the 28th of January to the 2nd of February 2019 to meet the biennial inspection requirement of resolution WHA60.1. On the 27th of January, the designated inspectors met for a pre-inspection consultation to review the agenda, inspection practices and inspection protocol.

3. Two representatives of the other repository participated in the inspection as observers, excluding closed discussions among the WHO inspection team and during delivery of the results and recommendations to the inspected repository. This is sharing best practices as well as to ensure parity and impartiality of the inspection.

INSPECTION PROGRAMME

4. By agreement with both repositories, the present inspection included the elements defined in the protocol used in the 2009, 2012, 2014 and 2016 inspections. The European Committee for Standardization (CEN) Workshop Agreement (CWA) 15793 (2011) was used exclusively to structure the inspection and to follow up previous "findings". The facilities were not assessed for conformity to the CWA.

5. The inspection team and repository representatives agreed to use a transparent rating scale to categorize the findings at the two repositories. To ensure clarity and a consistent approach, findings are categorized as follows:

- Observations are either positive remarks, including examples of robust controls or other best practices, or related issues that are not directly associated with biosafety and biosecurity.
- Priority 1 findings indicate that an improvement is advisable.
- Priority 2 findings indicate that a timely remedial measure is required.

- Priority 3 findings indicate that immediate corrective action is required.

Previous findings found to be ongoing at the next inspection will contribute to the prioritization of future findings and issues to be addressed in any subsequent action plans.

6. The inspection took place over six days and included a full one-day inspection of the physical maximum containment facility designated for research with variola virus, its supporting mechanical systems, the long-term specimen storage repository and the isolation hospital. Two inspection team members and one observer with proof of vaccinia vaccination in the preceding five years to meet internal requirements of VECTOR were permitted to enter the restricted-access, long-term variola virus specimen storage area.

7. The WHO inspection team heard presentations from, and held interactive discussions with, VECTOR staff. The team specifically requested records, regulatory instruments, institutional rules, instruction manuals and meeting minutes as necessary for detailed review. The inspection team viewed manuals, the layout of the facility, policies and explanations of the hierarchy of documents. The final day provided an opportunity to discuss and confirm the WHO inspection team's understanding, observations and recommendations, which the inspection team presented to VECTOR top management and senior technical staff.

8. The WHO inspection team made every effort to assess the facility, documents and current practices over a limited timeframe. As the facility was not operational due to scheduled maintenance, the team did not observe any practical work during the inspection. The inspection team appreciated the collaborative attitude and committed engagement of the VECTOR management team and all responsible staff throughout the inspection. Presented below are the results of the WHO inspection, the aim of which is to reduce risk and encourage further use of international best practices.

1. Biological risk management system

9. VECTOR representatives presented and provided documentation of the policies, processes and procedures supporting their biological risk management system within their facility. The inspection team reviewed the document hierarchy in terms of national and international regulations, resolutions and their interaction, industry-wide, regional and institutional. The team also examined responsibilities and accountability for biological risk management through a range of manuals, committee meeting minutes, institutional orders and other relevant documents (e.g. logbooks).

10. The biological risk management system and approval processes of VECTOR integrate senior management, the national regulatory authority and dedicated biosafety committee members, which were demonstrated through the provision of documentation including internal inspection audits for biosafety compliance and training records.

11. The inspection team did not have any concerns relating to the biological risk management system.

2. Risk assessment

12. VECTOR has a consistent documented risk assessment process in place which considers all potential hazards in a category system followed by decision on commencement of work and considers the risk assessment as a tool for improving procedures.

13. *Observation*: Following a recommendation of the WHO inspection in 2016[1], VECTOR performed a risk assessment related to ventilated animal hoods no longer in use, resulting in removal of the hoods from the maximum containment area.

14. *Observation*: VECTOR has introduced a logbook for negative impact or near-miss monitoring following a recommendation of the last inspection. Some examples of incidents which had occurred and measures taken to mitigate the identified risk were explained to the inspection team.

15. The inspection team did not have any concerns relating to risk assessment.

3. Pathogen and toxin inventory and information

16. VECTOR has a well-established process for recording and inventorying its working and archival variola virus collections. The inventory is checked twice a year by VECTOR with an annual report sent to WHO. Two inspectors and one observer visited the long-term storage area for the variola virus, whereas the area for storage of viral DNA and genomes was visited by the whole inspection team. All materials are logged and catalogued with individuals responsible for the accuracy of these collections. The inspection team reviewed the detailed policy and rigorous procedures for transferring virus or DNA.

17. The inspection team did not have any concerns relating to pathogen and toxin inventory and information.

4. General safety

18. The inspection team reviewed aspects on general safety throughout the visit.

19. *Previous finding (paragraph 22): "The inspection team highlighted concern regarding an open wiring method for telephone communication wires (which nominal voltage value does not exceed 12 V) on a panel noted in the laboratory-clothing cloakroom."* The open wiring was removed and telecommunication in general was changed to IP phone. The Finding is now closed.

20. *Priority 1 finding:* As formaldehyde is considered as a probable carcinogen, the inspection team recommends monitoring of formaldehyde concentration in the following situations: on opening steam-formaldehyde sterilizer, inside the pressure suit after steam formaldehyde decontamination, outside

[1] Report of the World Health Organization (WHO) Biosafety Inspection Team of the Variola Virus Maximum Containment Laboratories to the State Research Centre of Virology and Biotechnology ("SRC VB VECTOR"), Koltsovo, Novosibirsk Oblast, Russian Federation, 10-15 October 2016

containment area in adjacent rooms during the final fumigation, inside containment area 96 hours after final fumigation. The goal is to physically verify (measured) that all critical spots are ventilated sufficiently.

5. Personnel and competence

21. VECTOR staff presented the inspection team with information on occupational health and safety, briefings for newly hired personnel, initial workplace, annual refresher and ad hoc training, training records and competency assessment.

22. *Observation*: VECTOR has a long-term succession planning system in place with competent personnel to occupy positions when needed. A policy of pre-assigned deputies guarantees management continuity. Such policy intended to ensure robust continuity of operations is commendable.

23. The inspection team did not have any concerns relating to personnel and competence.

6. Good microbiological practices (GMP)

24. VECTOR provided manuals and processes of safe working practices including a comprehensive training programme reflecting a commitment to good microbiological practices, which the inspection team reviewed.

25. VECTOR showed that detailed SOPs are in place to ensure GMP. As an example, VECTOR provided the SOP for handling mice organ homogenates, which demonstrated the implementation of GMP.

26. The inspection team did not have any concerns relating to good microbiological practices.

7. Clothing and personal protective equipment

27. VECTOR personnel explained in detail the three different categories of personal protective equipment (PPE) for the various areas of the facility. The inspection team observed numerous items of PPE during the on-site facility inspection. VECTOR presented the procedures for suit donning and doffing, testing, use, maintenance, repair and replacement. Details of the procedure for post-use suit decontamination and the processes required for reuse were provided. The inspection team reviewed the logbooks used for signing equipment in and out and for repairs.

28. *Observation*: Working with an external partner, VECTOR developed and introduced new pressure suits and a rigorous training regime for their use. Additionally, the inspection team had an opportunity to see the PPE used for final decontamination or emergencies.

29. *Observation*: The inspection team recommended that VECTOR summarise the positive and negative experiences in the use of the pressure suits for the next inspection as part of the Plan-Do-Check-Act (PDCA) cycle.

8. Human factors

30. *Observation*: A no-blame culture combined with the duty to report occurrences in a timely manner is in place.

31. The inspection team had discussions with VECTOR on this element and the team did not have any concerns relating to human factors.

9. Healthcare

32. The inspection team discussed this element with medical staff during a visit to the designated isolation hospital for highly dangerous infections including observation of the technical floors for engineering control. This exclusive hospital makes it possible to accommodate VECTOR personnel conducting work with variola virus for quarantine and/or treatment. Discussions included procedures for how potentially exposed staff would enter the facility, procedures for caring for staff, the types of equipment including PPE used, and general operation and maintenance of the facility.

33. The process for decontamination of an isolation ward after hospitalisation of a patient infected with a category 1 pathogen, which in the Russian classification includes variola virus, was clarified.

34. Vaccination is mandatory every three years for personnel working with variola virus and every five years for all other staff within the facility. Personnel have their antibody titre checked after every vaccination and subsequently every year. A 21-day quarantine period after staff entry into the maximum containment facility is in place, during which travelling is prohibited for longer than one day outside Novosibirsk. Close monitoring of staff health involves annual medical examinations, daily health checks including twice-daily temperature checks for workers and staff associated with the variola programme and entering the maximum containment area. Medical follow-up procedures in case of potential exposure, including differential diagnosis to rule out smallpox, also are outlined.