From: [redacted]
To: GMP Compliance
Subject: Additional information from MHLW/PMDA: Suspension of Moderna vaccines for specific lots [SEC=OFFICIAL]
Date: Thursday, 2 September 2021 9:16:30 AM
Attachments: image002.png
image003.png
image005.png
E-Moderna-Takeda Joint Statement 20210901_formatted CLEAN_FINAL_s.docx

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Hi [redacted]

Please find below further info about the Moderna signal.

Kind regards

[redacted]

[redacted]

[redacted]
Regulatory Strengthening Section
Regional Regulatory Support
(Indo-Pacific Regulatory Strengthening Program |Regulatory Support & Safety Monitoring Program)
Therapeutic Goods Administration | Health Products Regulation Group
Australian Government Department of Health
T: [redacted] E: [redacted]
Location: Symonston FG
PO Box 100, Woden ACT 2606, Australia

The Department of Health acknowledges the traditional owners of country throughout Australia, and their continuing connection to land, sea and community. We pay our respects to them and their cultures, and to elders both past and present.

Dear ICMRA colleagues,

As a follow up to the information on the suspension of three lots of Moderna vaccine in Japan, I would like to share with you the latest joint-statement which has just been published by Takeda/Moderna. Please find attached.

The particles identified in lot 3004667 have been confirmed to be stainless steel.
The most probable root cause of the contamination is related to friction between two pieces of metal installed in the stoppering module of the production line due to an incorrect set-up occurred during a line changeover before starting the lot. The correction measures have been taken by ROVI.

The three suspended lots (3004667, 3004734, 3004956) will be soon recalled from Japan market.
At the present, MHLW/PMDA has not decided to take further regulatory action. But we will continue investigation and assessment, including the assessment of causal association between two death cases and the vaccination with the suspended lot, and take actions if necessary.

Note:
Some of the hyperlinks in the attached statement are linked to Japanese site. English sites are shown as below, for your easy reference.
- Announcement on August 26, 2021
https://www.takeda.com/ja-jp/announcements/notice-of-suspension-of-use-of-specific-lots-of-modernas-covid-19-vaccine-in-japan/
- Joint statement on August 28, 2021
https://www.takeda.com/ja-jp/announcements/moderna-and-takedas-response-to-the-incidents-announced/

Best regards,

[redacted]

[redacted]
Office of International Regulatory Affairs
Pharmaceutical Safety and Environmental Health Bureau
Ministry of Health, Labour and Welfare (MHLW), Japan
TEL: [redacted]
FAX: [redacted]

From: [redacted]
Sent: Monday, August 30, 2021 10:17:05 AM
To [redacted]

[redacted]

[redacted]

[redacted]

Cc [redacted]

Subject:【外部メール】RE: Additional information from MHLW/PMDA: Suspension of Moderna vaccines for specific lots

Dear colleagues,

I would like to make a correction.
Age of case 2 is 30 yrs old.

[redacted]

From: [redacted]
Sent: Saturday, August 28, 2021 3:16 PM
To [redacted]

[redacted]

[redacted]

Cc [redacted]

Subject: Additional information from MHLW/PMDA: Suspension of Moderna vaccines for specific lots

Dear colleagues,

MHLW/PMDA would like to share additional information regarding foreign materials contamination of Moderna vaccine.
MHLW/PMDA received two AEFI reports of fatal cases. Both are still under investigation, so the causal relationship with the vaccine is not clear currently.
The information of these cases area followings;

1. Case 1
   38 yrs old, male
   Underlying disease: no

Allergy history: no
Vaccination dates: 18th July (Lot 3004228) and 15th August (Lot 3004734)
Event date: 18th August
Time course after vaccination:
16th August Fever (38.5℃)
17th August Reduced fever
18th August Confirmed dead at home
Cause of death: under investigation (dissection)

2. Case 2
38 yrs old, male
Underlying disease: no
Allergy history: no
Vaccination dates: 18th July (Lot 3003657) and 22nd August (Lot 3004734)
Event date: 25th August
Time course after vaccination:
23rd August Fever, took day off work
24th August Cured, worked at office and went to bed after returning home
25th August Death was confirmed at morning

MHLW/PMDA is collecting additional data and will review the causal relationship with external experts.
We will continuously share the update on the issue.

[redacted]
****
[redacted]
Pharmaceuticals and Medical Devices Agency
3-3-2 Kasumigaseki Chiyoda, Tokyo, 100-0013, JAPAN
TEL: [redacted]
E-mail: [redacted]
****

From: [redacted]
Sent: Thursday, August 26, 2021 4:31 PM
To: [redacted]

[redacted]

Cc: [redacted]

Subject: ICMRA sharing information from MHLW/PMDA: Suspension of Moderna vaccines for specific lots

MHLW/PMDA would like to share latest information on Moderna vaccine.

Takeda Pharmaceutical co.ltd., which is marketing authorization holder of “COVID-19 Vaccine Moderna Intramuscular Injection” in Japan, reported to suspend the use of the specific lots (lot numbers - 3004667, 3004734 and 3004956) due to contamination of foreign materials. It is not recall. So far, MHLW and PMDA have not received any repots of safety concerns over this issue.
MHLW and PMDA will communicate with Takeda closely and make efforts not to affect the availability of coronavirus vaccine doses in the country.
If we have any update on this issues, we will let you know.

With my best regards,
[redacted]

****
[redacted]
Pharmaceuticals and Medical Devices Agency (PMDA)
3-3-2 Kasumigaseki, Chiyoda, Tokyo, 100-0013, Japan
TEL : [redacted]
FAX : [redacted]
E-mail : [redacted]
****

Better Health, Brighter Future

Joint Statement

Joint Statement from Moderna and Takeda on the Investigation of Suspended Lots of Moderna's COVID-19 Vaccine in Japan

Osaka, Japan, September 1 – *This statement updates the separate announcement on August 26, 2021, JST, in which Takeda announced the suspension of the use of three lots of the Moderna COVID-19 Vaccine for Intramuscular Injection in Japan following reports from vaccination sites of a potential foreign particulate substance found in vials. It also updates the joint statement on August 28, 2021, in which Takeda and Moderna confirmed that they were notified of the deaths of two individuals, both of whom received Moderna's COVID-19 vaccine in Japan from one of the three lots.*

Working with the Ministry of Health, Labour and Welfare (MHLW), Moderna, the vaccine manufacturer, ROVI Pharma Industrial Services, S.A. in Spain, Moderna's European contract manufacturing organization, and Takeda, the authorized distributor, have conducted a thorough investigation, which includes:

- Identification of the root cause of the particles and the corrective and preventive actions being taken;
- An assessment of the nature of a particle from one vial from Lot 3004667; and
- An associated medical safety assessment, to determine if the identified particle poses a health or safety risk.

Root Cause Investigation, and Corrective and Preventive Actions

Three lots of the Moderna COVID-19 Vaccine (Lots 3004667, 3004734 and 3004956) were suspended following reports from vaccination sites of a potential foreign particulate substance observed in unused vials from Lot 3004667.

According to the root cause analysis report, conducted by ROVI, the most probable cause of the particulates identified in lot 3004667 is related to friction between two pieces of metal installed in the stoppering module of the production line due to an incorrect set-up. The two pieces are the star-wheel and the stoppers feeding device piece which feeds stoppers into the star-wheel. It is believed that this condition occurred during the assembling of the line prior to production of batch 3004667 and was a result of improper alignment during a line changeover before starting this batch.

Based on the analysis conducted by ROVI, the manufacturing issue only impacted the lots that were included in the suspension. The following steps have been taken by ROVI to correct and prevent future defects:

- Full inspection of the manufacturing line;

- Improving standard operating procedure for changeover of manufacturing line; and
- Setting alert inspection limits in the automatic visual inspection, as an internal process control.

Takeda, as the Japan Marketing Authorization Holder, is planning to initiate the recall of the three suspended lots 3004667, 3004734, and 3004956 from the market as of September 2, 2021, in consultation with MHLW and reported to the Osaka Prefecture. Moderna as the Global Marketing Authorization Holder is in full agreement with this decision.

Preliminary Particulate Analysis

According to Moderna's independent analysis, the particle from lot 3004667 has been thoroughly analyzed and is confirmed to be grade 316 stainless steel. This is consistent with the root cause determination described above. Grade 316 is a high grade of stainless steel commonly used in manufacturing and in food processing.

Current Medical Safety Assessment

After a health assessment conducted by Moderna and Takeda, the rare presence of stainless steel particles in the Moderna COVID-19 vaccine does not pose an undue risk to patient safety and it does not adversely affect the benefit/risk profile of the product.

Metallic particles of this size injected into a muscle may result in a local reaction, but are unlikely to result in other adverse reactions beyond the local site of the injection. Stainless steel is routinely used in heart valves, joint replacements and metal sutures and staples. As such, it is not expected that injection of the particles identified in these lots in Japan would result in increased medical risk.

Investigation of Two Deaths Following Administration of Vaccine

At this time, there is no evidence that the two tragic deaths following administration of the Moderna COVID-19 vaccine (from lot 3004734) were in any way related to administration of the vaccine. The relationship is currently considered to be coincidental. It is important to conclude a formal investigation to confirm this. The investigation is being conducted with the greatest sense of urgency, transparency and integrity and is of the highest priority.

To date, more than 200 million doses of the Moderna COVID-19 vaccine have been administered to more than 110 million individuals in 45 countries, representing a critical component of the global fight against COVID-19.

For additional updates and resources about the COVID-19 vaccine program in Japan please go to the official COVID-19 information center.

About Takeda Pharmaceutical Company Limited

Takeda Pharmaceutical Company Limited (TSE: 4502/NYSE: TAK) is a global, values-based, R&D-driven biopharmaceutical leader headquartered in Japan, committed to discover and deliver life-transforming treatments, guided by our commitment to patients, our people and the planet. Takeda focuses its R&D efforts on four therapeutic areas: Oncology, Rare Genetic and Hematology, Neuroscience, and Gastroenterology (GI). We also make targeted R&D investments in Plasma-Derived Therapies and Vaccines. We are focusing on developing highly innovative medicines that contribute to making a difference in people's lives by advancing the frontier of new treatment options and leveraging our enhanced collaborative R&D engine and capabilities to create a robust, modality-diverse pipeline. Our employees are committed to improving quality of life for patients and to working with our partners in healthcare in approximately 80 countries. For more information, visit https://www.takeda.com.

Media Contacts:

Japanese Media

[redacted]

Media outside Japan

[redacted]

[redacted]

For Moderna Media Inquiries:

[redacted]

Forward-Looking Statements

This press release and any materials distributed in connection with this press release may contain forward-looking statements, beliefs or opinions regarding Takeda's future business, future position and results of operations, including estimates, forecasts, targets and plans for Takeda. Without limitation, forward-looking statements often include words such as "targets", "plans", "believes", "hopes", "continues", "expects", "aims", "intends", "ensures", "will", "may", "should", "would", "could" "anticipates", "estimates", "projects" or similar expressions or the negative thereof. These forward-looking statements are based on assumptions about many important factors, including the following, which could cause actual results to differ materially from those expressed or implied by the forward-looking statements: the economic circumstances surrounding Takeda's global business, including general economic conditions in Japan and the United States; competitive pressures and developments; changes to applicable laws and regulations, including global health care reforms; challenges inherent in new product development, including uncertainty of clinical success and decisions of regulatory authorities and the timing thereof; uncertainty of commercial success for new and existing products; manufacturing difficulties or delays; fluctuations in interest and currency exchange rates; claims or concerns regarding the safety or efficacy of marketed products or product candidates; the impact of health crises, like the novel coronavirus pandemic, on Takeda and its customers and suppliers, including foreign governments in countries in which Takeda operates, or on other facets of its business; the timing and

impact of post-merger integration efforts with acquired companies; the ability to divest assets that are not core to Takeda's operations and the timing of any such divestment(s); and other factors identified in Takeda's most recent Annual Report on Form 20-F and Takeda's other reports filed with the U.S. Securities and Exchange Commission, available on Takeda's website at: https://www.takeda.com/investors/sec-filings/or at www.sec.gov. Takeda does not undertake to update any of the forward-looking statements contained in this press release or any other forward-looking statements it may make, except as required by law or stock exchange rule. Past performance is not an indicator of future results and the results or statements of Takeda in this press release may not be indicative of, and are not an estimate, forecast, guarantee or projection of Takeda's future results.