From: [redacted]
To: [redacted]
Cc: [redacted]
Subject: FW: GMP non-compliance report for Rovi, Spain [SEC=OFFICIAL]
Date: Wednesday, 8 September 2021 8:09:33 AM
Attachments: image001.png
image002.jpg
image003.png
Executive Summary Report - Japan.pdf
image004.png
image005.png
image006.gif
image007.png

Hi [redacted]
Keeping you in the loop on the particles in Moderna's vaccine supplied to Japan.
In summary:

- Particles identified as stainless steel (no detail on how this was done)
- Root cause investigation indicated it was a mis-alignment of parts on the filling line causing abrasion;
- Implicated batch identified in Japan was the first batch manufactured in a campaign. 4 additional batches were manufactured prior to the issue being identified taking the total to 5 batches affected.
- Of the 5 batches 3 were released to Japan and 2 were not released by Moderna/ROVI. The 3 released batches have a recall issued in Japan
- Corrective actions have been put in place to address the filling line and also the automated visual inspection process.
- CAPAs are also being put in place for other filling lines used at the ROVI site for Moderna vaccine.

My interpretation is that the proposed root cause seems to have identified the issue and the CAPAs put in place should prevent the issue reoccurring. I will try and get some time to discuss with MQB colleagues who are likely to have better insight into the issue and the corrections.
Kind regards,

[redacted]

Medical Devices and Product Quality Division | Health Products Regulation Group
Laboratories Branch
Australian Government Department of Health
T: [redacted] | E: [redacted]
Location: TGA Symonston Building
PO Box 100, Woden ACT 2606, Australia

The Department of Health acknowledges the Traditional Custodians of Australia and their continued connection to land, sea and community. We pay our respects to all Elders past and present.

From: [redacted]
Sent: Tuesday, 7 September 2021 12:09 PM
To: GMP Compliance
Cc [redacted]
Subject: Re: GMP non-compliance report for Rovi, Spain [SEC=OFFICIAL]

Dear [redacted]
As requested, please find attached the risk assessment completed by the manufacturer. The summary is as below:

> Investigation of Complaint registered by Rovi the 24th of August, 2021 (ref. RC-298/21) related to the presence of foreign particles in several vials of batch number 3004667 of the product Covid-19 Moderna vaccine has concluded with the following findings:
> Batch number 3004667 was the first batch manufactured within a campaign of batches produced, from the 27th of June 2021 and finished the 27th of July.
> The investigation has revealed that, during the assembling of the elements of the line needed to produce first batch 3004667, there was a misalignment of two metallic elements of the line. The misalignment created friction between these elements, which has been identified as the most probable source of the foreign particles.
> The investigation has concluded that batches 3004667 (1st campaign batch), 3004734 (2nd campaign batch) and 3004956 (3rd campaign batch) are potentially impacted by this issue. An intervention in the line right after the production of batch 3004956 (3rd campaign batch) did not allow the detection of an abrasion in these elements of the line. Two additional batches were produced (numbers 3004957 and 3004958; 4th and 5th within this campaign). The abrasion was detected during production of batch 3004958; and then the alignment of the part was corrected on the 2nd of July. Batches 3004957 and 3004958 were never released to the market. Due to the sequence of interventions, the manufacturer concluded that the abrasion issue was limited to batch numbers 3004957 and 3004958. For this reason, the three first batches of the campaign (3004667, 3004734 and 3004956) were released.
> No further batches distributed in any market were produced with the misalignment of format parts as described above.
> Batches 3004667 (1st campaign batch), 3004734 (2nd campaign batch) and 3004956 (3rd campaign batch) were entirely distributed in Japan.

Please don't hesitate to reach out for any questions
Regards,
[redacted]

From: [redacted]
Sent: Thursday, September 2, 2021 8:26 AM
To: GMP Compliance <GMPCompliance@health.gov.au>
Cc: [redacted]

[redacted]

Subject: RE: GMP non-compliance report for Rovi, Spain [SEC=OFFICIAL]

EXTERNAL

Dear [redacted]

Further to the correspondence below, additional information was sent to the TGA Regulatory team overnight so I am sharing here to maintain all information in a single chain.

> As committed, we are sending a follow up statement that Moderna and Takeda, Moderna COVID-19 Vaccine Marketing authorization Holder in Japan, have issued today regarding the Investigation of Suspended Lots of Moderna's COVID-19 Vaccine, which were manufactured exclusively for Japan (Moderna's website).
>
> 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.
>
> Takeda 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 Osaka Prefecture.
>
> Moderna as the Global Marketing Authorization Holder is in full agreement with this decision.
>
> Please do not hesitate to reach out if you have any questions.

Regards,

[redacted]

[redacted]

www.adjutor.com.au

From: GMP Compliance <GMPCompliance@health.gov.au>
Sent: Thursday, 2 September 2021 8:02 AM
To: [redacted]
Cc: [redacted]

[redacted]

Subject: RE: GMP non-compliance report for Rovi, Spain [SEC=OFFICIAL]

Dear [redacted]

Thank you for providing the information below.

Please forward the information relating to the root cause and corrective actions taken as noted below.

I understand there are a number of interested parties in the TGA and I appreciate you keeping everyone informed of the on-going actions relating to this issue.

Kind Regards

[redacted]
Compliance Officer
Licensing and Compliance Strategy Section
Phone: 1800 020 653
Email: GMPCompliance@health.gov.au
Therapeutic Goods Administration
Department of Health
PO Box 100
Woden ACT 2606
www.tga.gov.au

Important information:

Guidance on management of GMP Signal has been published
The TGA have published guidance on how on the TGA manage GMP Compliance Signals for medicines and biologicals

TGA suspends overseas GMP inspections until further notice
Sponsors affected by the recent suspension of TGA GMP inspections have been contacted and advised about maintaining validity of their GMP Clearance(s).

TGA response to coronavirus (COVID-19) - GMP information for sponsors and manufacturers
If the COVID-19 outbreak results in delays to your GMP inspections, please ensure you maintain the validity of your GMP Clearance(s) and submit timely extension application(s).

Do you have a Good Manufacturing Practice licence or GMP Clearance?

Are you aware of your responsibilities to notify the TGA? Click here to see when and how to notify the TGA.

Did you know you should notify the TGA of any regulatory actions by any competent overseas regulatory authority (for example, recalls, unacceptable inspection findings, warning letters, import alerts etc.). Click here to see when and how to notify the TGA.

From: [redacted]
Sent: Wednesday, 1 September 2021 5:56 PM
To: GMP Compliance <GMPCompliance@health.gov.au>

Cc: [redacted]

Subject: RE: GMP non-compliance report for Rovi, Spain [SEC=OFFICIAL]

REMINDER: Think before you click! This email originated from outside our organisation. Only click links or open attachments if you recognise the sender and know the content is safe.

Dear TGA,

Attached please find the completed "GMP Compliance – Details of supply relating to a GMP non-compliance report" in response to the email below.

Regards,

[redacted]

www.adjutor.com.au

From: [redacted]
Sent: Tuesday, 31 August 2021 7:32 PM
To: GMP Compliance <GMPCompliance@health.gov.au>
Cc: [redacted]

Subject: RE: GMP non-compliance report for [Manufacturer][Country] [SEC=OFFICIAL]

Dear TGA,

As per previous correspondence, Moderna is actively working to provide the information that TGA has requested. The "GMP Compliance – Details of supply relating to a GMP non-compliance report" is undergoing legal review prior to return to TGA.

Investigation is ongoing and Moderna are expecting to have more information by the end of the week.

Regards

[redacted]

www.adjutor.com.au

From: [redacted]
Sent: Tuesday, 31 August 2021 11:29 AM

To: 'GMP Compliance' <GMPCompliance@health.gov.au>
Cc: [redacted]
Subject: RE: GMP non-compliance report for [Manufacturer][Country] [SEC=OFFICIAL]

Dear All,

In the interests of retaining all related communication in the one email chain, below is further correspondence from Moderna sent overnight.

> At this time I can confirm the following:
>
> - The complaints related to the suspension of the batches in Japan are related to one specific lot (Lot # 3004667)
>
> - Two adjacent lots manufactured in the same series (Lot # 3004734, and Lot # 3004956) were included in the suspension, out of an abundance of caution
>
> - We understand that the two individuals whose deaths were reported over the weekend in Japan received doses from Lot # 3004734
>
> - Based on the preliminary root cause analysis by our third party contract manufacturer, the issue is limited to lots produced exclusively for Japan, and to date there is no anticipated impact on any product supplied to other markets.
>
> We are working diligently on the investigation, and we will inform you timely as soon as we have new information.

Adjutor is awaiting feedback from Moderna regarding the ***GMP Compliance – Details of supply relating to a GMP non-compliance report*** and are intending to provide a response within the specified timeline.

Regards,

[redacted]
www.adjutor.com.au

From: [redacted]
Sent: Monday, 30 August 2021 8:45 AM
To: GMP Compliance <GMPCompliance@health.gov.au>
Cc: [redacted]
Subject: RE: GMP non-compliance report for [Manufacturer][Country] [SEC=OFFICIAL]

Dear [redacted]

Moderna are working on the ***GMP Compliance – Details of supply relating to a GMP non-compliance report*** and are intending to provide a response within the specified timeline. In the meantime, the follow update has been provided.

> "You may be aware of media reports over the weekend from Japan related to the unfortunate deaths of two individuals following administration of the Moderna vaccine.
>
> Although no product has been supplied to Australia yet, we wanted to make sure that you had seen the statement that we issued jointly with Takeda, the marketing authorization holder in Japan.
>
> https://investors.modernatx.com/news-releases/news-release-details/joint-statement-moderna-and-takeda
>
> As noted in the statement, the product lot in question was one produced by our European contract manufacturer on a line exclusively designated for Japan and we are working closely with Takeda and MHLW in our investigation.
>
> Patient safety and product quality remain the utmost top priorities for Moderna.
>
> We will therefore be providing additional updates as information becomes available and will forward those as well."

Regards,

[redacted]

[redacted]

www.adjutor.com.au

From: GMP Compliance <GMPCompliance@health.gov.au>
Sent: Friday, 27 August 2021 11:00 AM
To: [redacted]
Subject: GMP non-compliance report for [Manufacturer][Country] [SEC=OFFICIAL]

Dear All
The TGA have become aware of a GMP non-compliance at the site below following news reports of contamination in product (https://www.reuters.com/world/asia-pacific/japan-withdraws-16-mln-moderna-covid-19-vaccine-doses-over-contamination-nikkei-2021-08-25/) .

Rovi Pharma Industrial Services SA
Via Complutense 140 Alcala de Henares, Madrid 28805
Spain

A review of the information available to the TGA indicates that Moderna holds registrations /listing or applications (including clearance or product submissions) for this manufacturer. Sponsors have responsibilities to notify the TGA and provide information in relation to any potential adverse impact on quality, safety and efficacy of medicines supplied in Australia, including matters related to manufacturers of the medicines and API. Please advise if Moderna have advised the TGA of this issue and provide a copy of the correspondence.
Therefore, in relation to this manufacturing site:

1. Please complete the attached form (***GMP Compliance – Details of supply relating to a GMP non-compliance report – Details of supply relating to a GMP non-compliance report***) indicating supply of products into the Australian market, clearance information and product submissions, and return to the TGA by COB 31 August 2021

Please note that completing the attached form is the preferred format for providing information as it provides some guidance on the information to be provided to the TGA. However, you may provide equivalent information in other formats, if appropriate. For example, if you have provided a report to TGA Medicines Shortages where the report contains the same information, then such report may be provided to GMP Compliance instead of completing the form attached.

2. Please provide by COB 10 September 2021:

2.1. a detailed risk assessment as per PIC/S GMP Guide Annex 20 completed by the manufacturer for the products supplied and/or intended to be supplied to the Australian market which:

- addresses the issues above and
- Identifies root causes where applicable and outlines risk assessment, evaluation, rationale, corrective and preventative actions and/or risk mitigating strategies to support the continued supply of products from this site to Australia.

- For further information and guidance relating to quality risk assessment, please refer to ICH Q9 Quality Risk Management / PICS GMP Guide: Annex 20.

2.2. A summary of the CAPAs proposed, planned, implemented and the CAPA status update.

Please provide the above information by the due date/s indicated. Please note that after this due date, the compliance assessment process will progress and regulatory action/s may be taken if the information is not provided by the due date or does not adequately address the risks and the signal.

Please refer to the Guidance on the management of GMP Compliance Signals https://www.tga.gov.au/resource/guidance-management-gmp-compliance-signals for further information related to the TGA GMP Compliance framework.

If you have any questions in relation to this matter, please contact GMPCompliance@health.gov.au.

Please refer to the attached document for specific details and actions relating to the notice, including the due date for a response. Please note under the Electronic Transaction Act 1999, any notice sent via email is assumed to have been received by the sponsor once it is delivered to the sponsor's email address; not when it is opened by the sponsor.

The TGA will only be sending this letter via email so it is important that you keep your details up-to-date. If you wish to update your contact details with the TGA, please login to your account through TGA Business Services or contact the eBS Helpdesk on 1800 010 624 or eBusinessServices@health.gov.au.

For guidance on how your information will be treated by the TGA see: Treatment of information provided to the TGA at <https://www.tga.gov.au/treatment-information-provided-tga

Kind Regards

[redacted]
Compliance Officer
Licensing and Compliance Strategy Section
Phone: 1800 020 653
Email: GMPCompliance@health.gov.au
Therapeutic Goods Administration
Department of Health
PO Box 100
Woden ACT 2606
www.tga.gov.au

Important information:

Guidance on management of GMP Signal has been published

The TGA have published guidance on how on the TGA manage GMP Compliance Signals for medicines and biologicals

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SUMMARY

Investigation of Complaint registered by Rovi the 24th of August, 2021 (ref. RC-298/21) related to the presence of foreign particles in several vials of batch number 3004667 of the product Covid-19 Moderna vaccine has concluded with the following findings:

Batch number 3004667 was the first batch manufactured within a campaign of batches produced, from the 27th of June 2021 and finished the 27th of July.

The investigation has revealed that, during the assembling of the elements of the line needed to produce first batch 3004667, there was a misalignment of two metallic elements of the line. The misalignment created friction between these elements, which has been identified as the most probable source of the foreign particles.

The investigation has concluded that batches 3004667 (1st campaign batch), 3004734 (2nd campaign batch) and 3004956 (3rd campaign batch) are potentially impacted by this issue. An intervention in the line right after the production of batch 3004956 (3rd campaign batch) did not allow the detection of an abrasion in these elements of the line. Two additional batches were produced (numbers 3004957 and 3004958; 4th and 5th within this campaign). The abrasion was detected during production of batch 3004958; and then the alignment of the part was corrected on the 2nd of July. Batches 3004957 and 3004958 were never released to the market. Due to the sequence of interventions, the manufacturer concluded that the abrasion issue was limited to batch numbers 3004957 and 3004958. For this reason, the three first batches of the campaign (3004667, 3004734 and 3004956) were released.

No further batches distributed in any market were produced with the misalignment of format parts as described above.

Batches 3004667 (1st campaign batch), 3004734 (2nd campaign batch) and 3004956 (3rd campaign batch) were entirely distributed in Japan.

1. INVESTIGATION

On 24/08/2021 the Moderna complaint was registered by the QA Dpt. of Rovi Pharma Industrial services, S.A.U., regarding batch 3004667 of Covid-19-vaccine (SCAR QE-009191) RC-298/21. The wording of the complaint is:

- *QE-009172: Dr Hori from Waseda University Workplace Vaccination site has reported (7) vials with particulates for batch 3004667.*

The batch 3004667 of Covid-19 Moderna vaccine was manufactured by Rovi Pharma Industrial Services, S.A.U. (Rovi from now on) in the manufacturing site los San Sebastián de los Reyes (Madrid, Spain) in a production line called "Marchesini". The batch was fully distributed in Japanese market. The MAH is Takeda Pharmaceutical Company Limited.

Later to this complaint a market action was authorized by the Japanese Sanitary Authorities – PMDA -. The market action involves three batches, which are:

- Batch number 3004667 (Rovi Bulk batch 3004621 and **1st batch** within this campaign).
- Batch number 3004734 (Rovi Bulk batch 3004704, and **2nd batch** within this campaign).
- Batch number 3004956 (Rovi Bulk batch 3004926, and **3rd batch** within this campaign).

1. ROOT CAUSE INVESTIGATION:

The different steps of the manufacturing process, utilities, auxiliary equipment and elements of the vials filing line were investigated to ensure compliance with the specifications and the applicable instructions and protocols as well as with GMPs. The vials corresponding to the batches affected of "Covid-19 Moderna vaccine" are dosed, stoppered, and capped in the manufacturing line called "Marchesini". The line and other elements were investigated, with the following conclusions.

s47