

External Q&A

Information on MVA-BN Drug Product

Storage Temperatures, Shelf Life, Shipment and Supportive Temperature Excursion Information

Regulatory Affairs, Bavarian Nordic

1 Introduction

The information in this Q&A is provided “as is” and without liability to Bavarian Nordic (BN). This Q&A is valid from 07-June-2022 (Version 1.0). BN undertakes no obligation to update the information or inform of changes hereto. The information is confidential, is not to be redistributed and must only be used for the sole purpose of assessing whether to buy products from BN. The information does not constitute and is not to be construed as a guarantee, warranty or representation of any kind. This Q&A does not constitute an offer of BN to sell or deliver products. Any purchase of products from BN will be subject to negotiation and execution of a supply agreement.

2 Information on Approved Storage Temperatures and Shelf Life

The following table provides an overview of approved drug product (DP) storage temperatures and shelf life for different markets.

Table 1 Overview of approved DP Shelf Life in different Markets

Storage Temperature	Market	Approved Shelf Life
-20°C ± 5°C	US	3 years
	EU/UK	2 years*
	CAN	2 years*
-50°C ± 10°C	US	5 years
	EU/UK	5 years
	CAN	2 years**
-80°C ± 10°C	US	N/A***
	EU/UK	5 years***
	CAN	9 years

* Data available to support a shelf life extension to 3 years

** Data available to support a shelf life extension to 5 years

*** Data available to support a shelf life extension to 9 years

3 Shipment

Shipment of DP should be performed at ≤-15°C and take not more than 72 hours.

4 Question and Answers

The following Q&As deal with excursions and supportive data that BN has collected based on studies set up to provide information on stability in various scenarios. Not all the data have been submitted or have been approved by all authorities and as such should be used at the customers own risk/initiative.

Q1: Stability at 2-8°C after storage at -20°C, -50°C, -80°C?

A: After storage at -50°C, a maximum of 24 weeks at 2-8°C within product shelf life prior to use is approved for JYNNEOS by FDA.

After storage at -20°C, a maximum of 8 weeks at 2-8°C after end of shelf life, prior to use is approved for IMVANEX by EMA.

After storage at -20°C, a maximum of 2 weeks at 2-8°C after end of shelf life, prior to use is approved for IMVAMUNE by HC.

Q2: Can JYNNEOS be stored at -80°C?

A: Yes, JYNNEOS can be stored at -80°C. Data are available that supports storage at -80°C, but it is not yet approved by FDA. However, a shelf life of 9 years has been approved for IMVAMUNE by Health Canada, and for IMVANEX, a 5-year shelf life at -80°C has been approved by EMA.

Q3: How long does it take to thaw a vial at ambient temperature?

A: If taken from -80°C: app. 10 minutes. If taken from -50°C or -20°C: Less than 10 minutes

Q4: How does it affect product shelf life, if the product is moved from -80°C or -50°C to -20°C?

A: Removing product from a storage temperature to a higher storage temperature, will shorten the shelf life. The new shelf life will be that of the new (higher) storage temperature, starting from the manufacturing date and not from the time the product is moved.

In Europe and Canada, a shelf life of 2 years at -20°C is approved. There are however real time data to support a shelf life of 3 years when stored at -20°C. This 3-year shelf life at -20°C is approved in the US for JYNNEOS. If Canadian and European customers choose to use the shelf life according to the US label, they should be aware of these differences in the approvals by their national authority. Exemptions for use might need to be requested.

Q5: Are there any data available on number and duration of excursions at ambient temperature ($20^{\circ} \pm 5^{\circ}\text{C}$)?

A: we have supportive data to show that up to 2 x 30 minute excursions of either $2-8^{\circ}\text{C}$ or $+20^{\circ}\text{C}$ does not have an impact on long-term stability when product is subsequently returned to either short- or long-term storage at -20°C . This is not approved by any authority however data are described in the dossiers.

Q6: Can product be shipped at $2-8^{\circ}\text{C}$ before use?

A: If previously stored at $-20^{\circ}\text{C} \pm 5^{\circ}\text{C}$, we have data to support that the vaccine can be stored short-term in a refrigerator at $2-8^{\circ}\text{C}$ for up to 8 weeks (EMA) or up to 2 weeks (HC) prior to use, while maintaining stability. The product should be stored in the original package in order to protect from light. The product can be shipped during this period as long as the shipment is also at $2-8^{\circ}\text{C}$, the product is still within overall shelf life.

For product stored at -50°C the allowed time at $2-8^{\circ}\text{C}$ is 24 weeks *within* the -50°C shelf life, this is approved for JYNNEOS by the FDA

Q7: When keeping the pack in a -20°C freezer, is it possible to take any individual vials out of the pack to move to $+2-8^{\circ}\text{C}$ but leaving the remainder of the pack in the freezer to maximise shelf life. Would this cause any concerns? Is there a specific time limit within which you can remove product from the freezer to remove individual vials before returning the pack to the freezer?

A: We do not recommend taking the package in and out of the freezer to remove vials. If vials can be removed individually from the freezer without disturbing the rest of the pack, there should not be any issue with doing it this way. However, this is under the condition that the freezer is not opened and closed so frequently during the day that the temperature cannot be considered as staying overall at $-20^{\circ}\text{C} (\pm 5^{\circ}\text{C})$. Any individual vials that are stored according to specifications should have the shelf life specified according to the storage temperature.

Q8: Are there any data or concerns related to stability and/or the fact that it is a live vaccine, if the vaccine is drawn up in the syringe 1-2 hours before a patient receives the shot?

A: After storage at -20°C you can keep the vaccine at $2-8^{\circ}\text{C}$ for a minimum of 2 weeks and still remain within shelf life. If stored at -50°C you can keep the vaccine at $2-8^{\circ}\text{C}$ for up to 24 weeks, if still within the overall shelf life at -50°C . With regards to room temperature please see **Duration of excursions at up to $+20^{\circ}\text{C} (\pm 3^{\circ}\text{C})$**

No data are available for keeping the product in the syringe before use. It is recommended to store the DP at $2-8^{\circ}\text{C}$ until right before use, and not drawing up the product into the syringe until right before use.

Q9: Do you have any stability data regarding drug product outside of 2-8°C?

A: Data are available to support a total of 1 hour (or 2 x ½ hour) at +20°C (±3°C) without impact on long-term stability of the product.

Q10: The label expiration is set to e.g. 09/2022 when is the exact expiration date?

A: The product will expiry end of the calendar month, in this case end of September 2022.

Q11: Doses stored at -50°C ± 10°C to be shipped below -15°C. Should they completely reach the shipping temperature before shipping?

A: It is fine to ship product taken directly from -50°C before it's temperature reaches -20°C (±5°C) during transport. The closer the shipment temperature is to actual storage temperature, the better, but shelf life is based on shipment of maximum -15°C. If temperature excursions should happen, data are available that may support this, see section on temperature excursions.

Q12: Must they go directly from production to -50°C or can they be stored at -20°C first and to save time ship directly from -20°C storage and not -50°C?

A: The shelf lives of product stored at -50°C are calculated based on an initial maximum 3 months at -20°C after production, so the product can be shipped directly, if overall -20°C storage and shipment does not exceed 3 months.

Q13: If you receive JYNNEOS batches that are labelled for storage at -20°C with a corresponding shelf life of 3 years as approved by FDA and then transfer these batches to storage at -50°C or -80°C what will the remaining shelf life be?

A: In general, the shelf life is calculated based on the date of manufacturing for the respective storage temperature. A general statement of impact on shelf life when product is moved from one temperature to the other is not possible.

Q14: For drug product stored in long-term frozen storage at -20°C, how can the product be shipped and stored prior to use?

A: For operational flexibility, drug product may be shipped either frozen at -20°C (-4°F) or refrigerated at 2-8°C (36–46°F) during an event depending on freezer capacity at the receiving site(s). Upon receipt the vaccine can be stored as follows:

- If vaccine is shipped frozen at -20°C and requires storage before use, maintain:
 - o Frozen (-20°C), if freezer capacity is available; OR
 - o Refrigerated (2-8°C). Do not refreeze.

- If vaccine is shipped at 2-8°C and requires storage before use, maintain refrigerated at 2-8°C. Do not refreeze.

Unopened vials of drug product may be stored at 2-8°C up to 2-8 weeks from thawing (see Q1). This information has been provided by the vaccine manufacturer based on available supportive stability data.

Please be aware that this differs from the storage and use by period of 12 hours once thawed that is found in the JYNNEOS package insert (Sections 2.2. Preparation and Administration and 16.2 Storage Conditions).

If stored frozen (-20°C), the vaccine should be used within the printed expiration date on the carton. Please note that the expiration date is not shown on the individual vial.”