Regulatory Challenges for Post-approval Changes of Nasal Suspension/Solution Products

ABOUT THIS SURVEY

ABOUT

The objective of this survey is to better understand the challenges of post-approval changes for nasal suspension and solution products when manufacturers of new drugs and generic products need to make changes in products after approvals of the applications. The results of the survey will be used by PQRI to identify topics for further discussion, research, and or potential workshops. The results of this survey will also be shared with FDA, which is a member of PQRI, for awareness of challenges with post-approval changes for nasal suspension and solution products.

INSTRUCTIONS

This survey is being conducted according to PQRI's Antitrust Guidelines. Please do NOT disclose names of any compounds, partners (e.g., companies, contractors, vendors, universities, or other collaborators), or other proprietary information. Please do not disclose any information that could identify a study subject, patient, investigator, healthcare provider, or consumer.

Please ensure that you have all necessary permissions and approvals from your company to respond to this survey and do NOT disclose any information your company would not want disclosed, even if in a form not attributable to your company.

SAVING THE SURVEY FOR LATER

If you need to stop the survey for any reason and wish to complete it later, you can save your responses and pick up where you left off. To save and exit, click the "Save and Continue Later" option displayed in the gray bar at the bottom of the survey browser window. You will be prompted to enter your email address and will receive a unique link, which will allow you to complete your responses at a later time.

SURVEY DEADLINE

Please provide your feedback by June 3, 2024

Questions about the administration of or content within this survey may be directed to PQRI's Secretariat (Jillian.Brady@faegredrinker.com).

Contact Information

1. **Please provide your contact information.**

Although the survey asks for your name and your company affiliation, the PQRI Secretariat will remove this information before sharing the anonymized aggregated results. Your responses will not be identified as coming from your company. The PQRI Secretariat is the only party who can link individual survey responses to responding companies and individuals and can follow-up with companies to clarify responses if needed. The PQRI Secretariat may also redact, anonymize, or aggregate responses to help protect the confidentiality of survey respondent's identities.

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First Name

Last Name

Company Name

Email Address

Definitions

This survey asks questions about post-approval changes for nasal solution/suspension products and bridging studies conducted to support those changes. For the purposes of this survey, nasal solution/suspension products and bridging studies are defined as follows:

- **Nasal solution/suspension products**: Nasal products that contain active pharmaceutical ingredients (API) dissolved or suspended in a formulation in nasal metered dose inhalers (MDIs) or metered-dose spray pumps.
- **Bridging Study**: A supplemental study performed to provide additional data to allow extrapolation of the existing data from the current product to that with changes. The bridging studies referenced in this survey include studies on quality and bioequivalence to support the change.

Background

2. Which of the following best describes your professional affiliation?

- ○ Pharmaceutical Industry
- ○ Consultant
- ○ Other - Please specify

3. What type of nasal solution/suspension products does your company or the companies you consult for currently manufacture? Please select all that apply.

- ☐ Brand name products
- ☐ Generic products

4. What is the size of your company?

- 1 - 100 employees
- 101 – 1,000 employees
- 1001 – 10,000 employees
- More than 10,000 employees

Nasal Suspension / Spray Post-Approval Changes

Show/hide trigger exists.

5. For nasal suspension/solution products, what kinds of post-approval changes has your company attempted to make or successfully made in the last 5 years? Please select all that apply.

- Changes related to **API**
- Changes related to the **Drug Product**
- Changes related to the **Device**
- None of the above

Active Pharmaceutical Ingredient (API) Post-Approval Changes

Page entry logic:
This page will show when: #5 Question "For nasal suspension/solution products, what kinds of post-approval changes has your company attempted to make or successfully made in the last 5 years? Please select all that apply. " is one of the following answers ("Changes related to **API**")

Show/hide trigger exists.

6. For nasal suspension/solution products, what kinds of post-approval changes related to **APIs** has your company made or attempted to make in the past 5 years? Please select all that apply.

Note - For each option you select below, you will be asked a series of questions

- Post-approval API supplier change
- Post-approval API specification change
- Post-approval API analytical method change
- Post-approval change in methods or materials for manufacturing API, such as equipment, process, scale
- Post-approval change of API manufacturing facility or addition of an alternate facility
- Post-approval change of API stability protocol
- Post-approval change in API comparability protocol
- Other - Please specify
- None of the above

Page description:
The following questions relate to the **[QUESTION #6 ANSWER CHOICE]** your company has or is currently in the process of making.

Page exit logic: Skip / Disqualify Logic
IF: #6 Question "For nasal suspension/solution products, what kinds of post-approval changes related to**APIs** has your company made or attempted to make in the past 5 years? Please select all that apply " is one of the following answers ("None of the above") **THEN:** Jump to page 8 - Comparability Protocols Use in Active Pharmaceutical Ingredient (API) Post-Approval Changes

7. In the past 5 years, has your company experienced any challenges determining the type of bridging study needed to satisfy regulatory agency acceptance of a [QUESTION #6 ANSWER CHOICE]? If yes, please describe the types of studies that did not satisfy FDA's requirements.

- ○ Yes, please describe.
- ○ No

8. In the past 5 years, has your company experienced any of the following challenges executing the type of bridging study needed to satisfy regulatory agency acceptance of a [QUESTION #6 ANSWER CHOICE]? Please select all that apply and use the text box to elaborate on the challenges faced.

- ☐ No regulatory recommendations available
- ☐ Lack of expertise in conducting the bridging study
- ☐ Lack of tools/instructions needed to conduct bridging study
- ☐ Insufficient access to API information from supplier to conduct the bridging study
- ☐ Other challenge(s)
- ☐ None of the above

Comparability Protocols Use in Active Pharmaceutical Ingredient (API) Post-Approval Changes

Page entry logic:
This page will show when: #6 Question "For nasal suspension/solution products, what kinds of post-approval changes related to **APIs** has your company made or attempted to make in the past 5 years? Please select all that apply." is one of the following answers ("Post-approval change in API comparability protocol")

VALIDATION Must be numeric

9. Approximately how many times has your company used a comparability protocol (CP) to implement post-approval changes related to nasal solution/suspension product APIs? Please respond with a number from 0 - 100. Please use the comment box below to elaborate.

Comments

LOGIC Show/hide trigger exists. Hidden unless: #6 Question "For nasal suspension/solution products, what kinds of post-approval changes related to **APIs** has your company made or attempted to make in the past 5 years? Please select all that apply." is one of the following answers ("Post-approval change in API comparability protocol")

10. How has your company submitted the CP for post-approval changes related to nasal solution/suspension product APs?

- Submitted the CP in an original application
- Submitted the CP in a prior approval supplement to an approved application
- Both
- Neither

LOGIC Hidden unless: #10 Question "How has your company submitted the CP for post-approval changes related to nasal solution/suspension product APs?" is one of the following answers ("Submitted the CP in a prior approval supplement to an approved application","Both")

11. Please describe why and under what circumstances your company has submitted the comparability protocol (CP) in a prior approval supplement (PAS) to an approved application.

Active Pharmaceutical Ingredient (API) Post-Approval Changes

Page entry logic:
This page will show when: #5 Question "For nasal suspension/solution products, what kinds of post-approval changes has your company attempted to make or successfully made in the last 5 years? Please select all that apply. " is one of the following answers ("Changes related to **API**")

12. In general, where has your company sought guidance when they've experienced challenges making post-approval changes related to nasal suspension/solution product **APIs**? Please select all that apply.

- ☐ Internal company expertise
- ☐ Consultants
- ☐ CRO or specialized lab service provider
- ☐ Regulatory guidances
- ☐ Controlled correspondences to FDA
- ☐ USP
- ☐ Other - Please specify
- ☐ Not applicable
- ☐ None of the above

Drug Product Post-Approval Changes

Page entry logic:
This page will show when: #5 Question "For nasal suspension/solution products, what kinds of post-approval changes has your company attempted to make or successfully made in the last 5 years? Please select all that apply. " is one of the following answers ("Changes related to the **Drug Product**")

13. For nasal suspension/solution products, what kinds of **drug product** post-approval changes has your company made or attempted to make in the past 5 years? Please select all that apply.

Note - For each option you select below, you will be asked a series of questions

- ☐ Post-approval excipient source change
- ☐ Post-approval excipient specifications and analytical method change
- ☐ Post-approval formulation composition change (including addition of new strengths)
- ☐ Post-approval drug product manufacturing site change or addition of alternate site/facility
- ☐ Post-approval product batch size change
- ☐ Post-approval product in-process specifications change
- ☐ Post-approval product specification change
- ☐ Post-approval product analytical method change
- ☐ Post-approval change of stability protocol
- ☐ Post-approval change of testing methods (e.g., manual actuations vs automated)
- ☐ Post-approval product shelf-life change
- ☐ Post-approval change to comparability protocol
- ☐ Other - Please specify
- ☐ None of the above

Page description:
The following questions relate to the **[QUESTION #13 ANSWER CHOICE]** your company has or is currently in the process of making.

14. In the past 5 years, has your company experienced any challenges determining the type of bridging study needed to satisfy regulatory agency acceptance of a [QUESTION #13 ANSWER CHOICE]? If yes, please provide information the specific types of the studies conducted that did not satisfy FDA's requirements.

- Yes (please describe)
- No

15. In the past 5 years, has your company experienced any of the following challenges executing the type of bridging study needed to satisfy regulatory agency acceptance for a [QUESTION #13 ANSWER CHOICE]? Please select all that apply. You may also use the text box to elaborate on the specific challenges faced.

- [ ] No regulatory recommendations available
- [ ] Lack of expertise in conducting the bridging study
- [ ] Lack of tools/instructions needed to conduct the bridging study
- [ ] Insufficient access to information needed to conduct the bridging study (e.g., excipient information)
- [ ] Other challenge(s)
- [ ] None of the above

Comparability Protocols Use in Drug Product Post-Approval Changes

Page entry logic:
This page will show when: #13 Question "For nasal suspension/solution products, what kinds of **drug product** post-approval changes has your company made or attempted to make in the past 5 years? Please select all that apply." is one of the following answers ("Post-approval change to comparability protocol")

VALIDATION Must be numeric

16. Approximately how many times has your company used a comparability protocol (CP) to implement post-approval changes to nasal solution/suspension drug products? Please respond with a number from 0 - 100. Please use the comment box below to elaborate.

Comments

LOGIC Show/hide trigger exists.

17. How has your company submitted the CP for post-approval changes related to nasal solution/suspension drug products?

- ○ Submitted the CP in an original application
- ○ Submitted the CP in a prior approval supplement to an approved application
- ○ Both
- ○ Neither

LOGIC Hidden unless: #17 Question "How has your company submitted the CP for post-approval changes related to nasal solution/suspension drug products?" is one of the following answers ("Submitted the CP in a prior approval supplement to an approved application","Both")

18. Please describe why and under what circumstances your company has requested a comparability protocol (CP) in a prior approval supplement (PAS) to an approved application.

Drug Product Post-Approval Changes

Page entry logic:
This page will show when: #5 Question "For nasal suspension/solution products, what kinds of post-approval changes has your company attempted to make or successfully made in the last 5 years? Please select all that apply. " is one of the following answers ("Changes related to the **Drug Product**")

19. In general, where have you/your company sought guidance when you've experienced challenges making post-approval changes related to nasal suspension/solution **drug products**? Please select all that apply.

- ☐ Internal company expertise
- ☐ Consultants
- ☐ CRO or specialized lab service provider
- ☐ Regulatory guidances
- ☐ Controlled correspondences to FDA
- ☐ USP
- ☐ Other - Please specify
- ☐ Not applicable
- ☐ None of the above

Device Post-Approval Changes

Hidden unless: #5 Question "For nasal suspension/solution products, what kinds of post-approval changes has your company attempted to make or successfully made in the last 5 years? Please select all that apply. " is one of the following answers ("Changes related to the **Device**")

20. For nasal suspension/solution products, what kinds of post-approval changes related to **device constituent parts** has your company made or attempted to make in the past 5 years? Please select all that apply.

Note - For each option you select below, you will be asked a series of questions

- [ ] Post-approval gasket elastomer material (stem gasket, neck gasket or floating gasket) change
- [ ] Post-approval actuator change
- [ ] Post-approval spray pump dip-tube change
- [ ] Post-approval bottle change
- [ ] Post-approval material supplier change
- [ ] Post-approval component specification change
- [ ] Post-approval change in device due to concerns on human factors
- [ ] Other - Please Specify
- [ ] None of the above

Page description:
The following questions relate to the **[QUESTION #20 ANSWER CHOICE]** your company has or is currently in the process of making.

21. In the past 5 years, has your company experienced any challenges determining the type of bridging study needed to satisfy regulatory agency acceptance of a [QUESTION #20 ANSWER CHOICE]? If yes, please provide information the specific types of the studies conducted that did not satisfy FDA's requirements.

- ○ Yes (please describe)
- ○ No

22. In the past 5 years, has your company experienced any of the following challenges executing the type of bridging study needed to satisfy regulatory agency acceptance of a [QUESTION #20 ANSWER CHOICE] ? Please select all that apply and use the text box to elaborate on the specific challenges faced.

- [ ] No regulatory recommendations available
- [ ] Lack of expertise in conducting the bridging study
- [ ] Lack of tools/instructions needed to conduct the bridging study
- [ ] Other challenge(s)
- [ ] None of the above

Device Post-Approval Changes

Page entry logic:
This page will show when: #5 Question "For nasal suspension/solution products, what kinds of post-approval changes has your company attempted to make or successfully made in the last 5 years? Please select all that apply. " is one of the following answers ("Changes related to the **Device**")

23. For changes to nasal spray pump components that are considered product contact, would you normally conduct product stability studies to support the change?

- Yes
- No

24. For changes to nasal spray pump components that are considered product contact, would you consider conducting extractable/leachable (E&L) studies in lieu of accelerated condition/room temperature stability studies to support the change? If yes, please use the comment box below to describe for which types of changes you would consider conducting E&L studies only.

- Yes
- No

Comments

25. Some USP general chapters, such as <661>, <87> and <88>, provide recommendations related to device material changes. Do you think additional recommendations for device material changes are needed? If yes, please use the text box below to elaborate.

- Yes
- No

Comments

Device Post-Approval Changes

Page entry logic:
This page will show when: #5 Question "For nasal suspension/solution products, what kinds of post-approval changes has your company attempted to make or successfully made in the last 5 years? Please select all that apply. " is one of the following answers ("Changes related to the **Device**")

26. In general, where has your company sought guidance when they've experienced challenges making post-approval changes related to nasal suspension/solution product **device constituent parts**? Please select all that apply.

- [ ] Internal company expertise
- [ ] Consultants
- [ ] CRO or specialized lab service provider
- [ ] Regulatory guidances
- [ ] Controlled correspondences to FDA
- [ ] USP
- [ ] Other. Please specify.
- [ ] Not applicable
- [ ] None of the above

Labeling Changes

27. Based on your understanding, what kinds of post-approval changes for nasal suspension/solution products would involve product labeling changes? Please select all that apply and use the text box next to each to provide more information, as appropriate.

- [ ] None of the below

API Post-Approval Change

- [ ] API supplier change
- [ ] API specification change
- [ ] API analytical method change
- [ ] Manufacture change, such as equipment, process, scale
- [ ] Change of facility or addition of alternate facility for API manufacture
- [ ] Change of post-approval stability protocol
- [ ] Changes in approved comparability protocols

Drug Product Post-Approval Change

- [ ] Excipient source change
- [ ] Excipient specifications and analytical method change
- [ ] Formulation composition change (including addition of new strengths)

- [ ] Drug product manufacturing site change or addition of alternate site/facility
- [ ] Product batch size change
- [ ] Product in-process specifications revision
- [ ] Product specification revision
- [ ] Product analytical method change
- [ ] Change of post-approval stability protocol
- [ ] Changes to approved comparability protocols
- [ ] New testing methods (e.g., manual actuations vs automated)
- [ ] Product shelf-life change

Device Post-Approval Change

- [ ] Gasket elastomer material change (stem gasket, neck gasket or floating gasket)
- [ ] Actuator change
- [ ] Spray pump dip-tube change
- [ ] Bottle change
- [ ] Material supplier change
- [ ] Component specification change

Other Post-Approval Change

- [ ] Other - Write In (Required) *

(untitled)

28. Which of the following supports would you find most helpful in addressing challenges associated with post-approval changes for nasal solution/suspension products? Please select all that apply.

- [ ] Regulatory guidances
- [ ] USP chapters
- [ ] Workshops or trainings
- [ ] Other - Please specify
- [ ] Not applicable

Comments

Thank You!

Thank you for taking our survey. Your response is very important to us.