

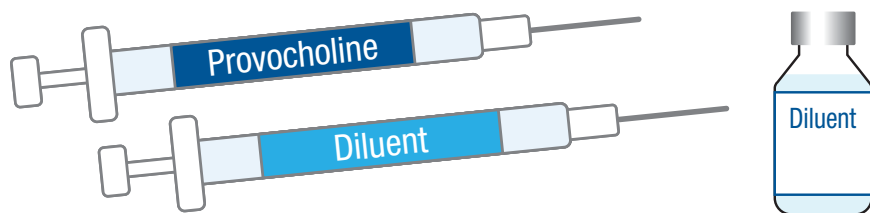
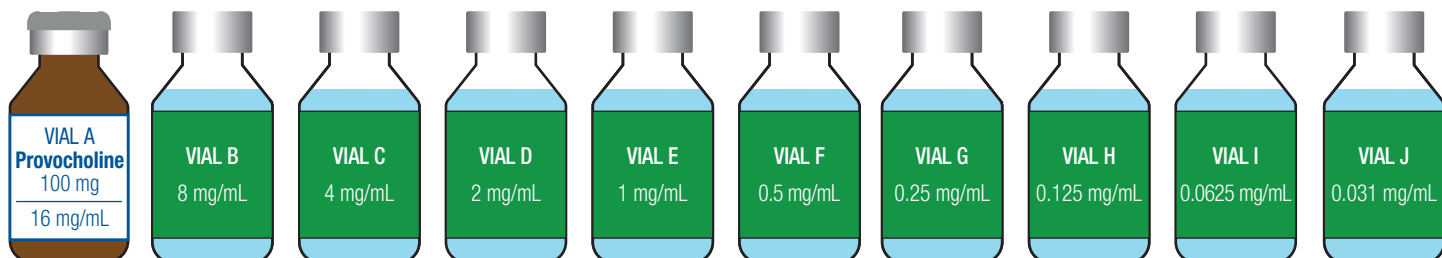
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Steps to Diluting Methacholine Chloride ATS “Long” - Doubling Doses

Dilution Sequence Protocol for Provocholine 100 mg/vial (US NDC № 64281-100-06)

Getting Started

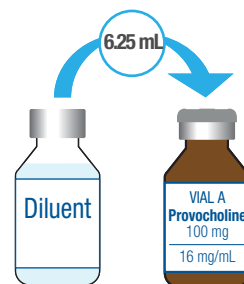
1. Attach labels to the vials.
2. Wipe down the stoppers of the Provocholine vial, diluent vial(s), and sterile empty vials with alcohol prep pads.
3. Label two (2) appropriately sized syringes (one for Provocholine, one for diluent), and attach needles to each.



1 Preparing Vial A

16 mg/mL Solution

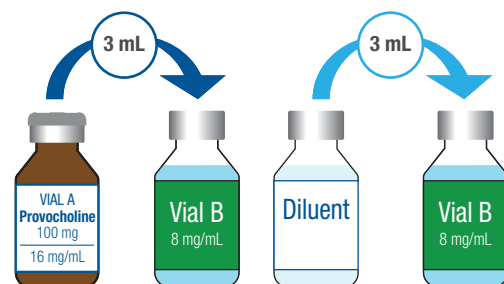
1. Using the diluent needle and syringe, draw 6.25 mL of the diluent and transfer to the Provocholine 100 mg vial.
2. Shake well.



2 Preparing Vial B

8 mg/mL Solution

1. Using the Provocholine needle and syringe, draw 3 mL from Vial A (16 mg/mL) and transfer to Vial B.
2. Using the diluent needle and syringe, draw 3 mL of diluent and transfer to Vial B.
3. Shake well.



Provocholine[®]
(methacholine chloride)

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NOTE

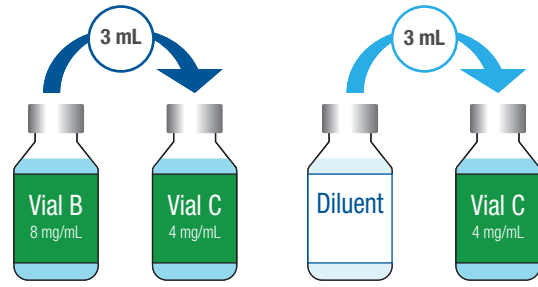
1. Transfer all dilutions (in vials A through E) to nebulizer through the 0.22 µm sterile bacterial retentive filter (Millex GV®).*
2. Be sure to follow your institutional policy for needle and sharps safety.

*Do not attach filter until AFTER solution has been drawn into syringe.

3 Preparing Vial C

4 mg/mL Solution

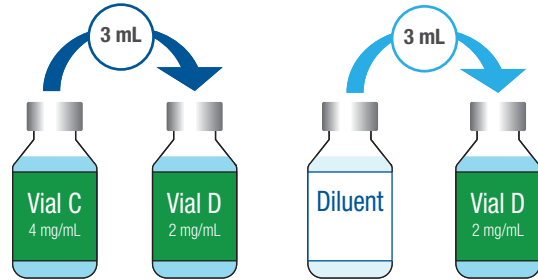
1. Using the Provocholine needle and syringe, draw 3 mL from Vial B (8 mg/mL) and transfer to Vial C.
2. Using the diluent needle and syringe, draw 3 mL of diluent and transfer to Vial C.
3. Shake well.



4 Preparing Vial D

2 mg/mL Solution

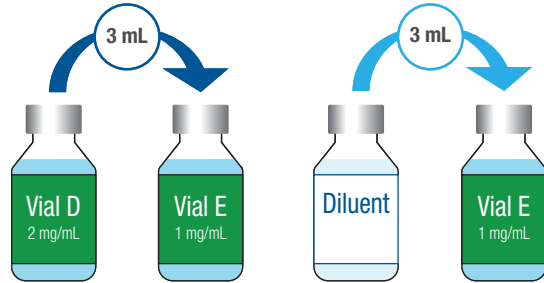
1. Using the Provocholine needle and syringe, draw 3 mL from Vial C (4 mg/mL) and transfer to Vial D.
2. Using the diluent needle and syringe, draw 3 mL of diluent and transfer to Vial D.
3. Shake well.



5 Preparing Vial E

1 mg/mL Solution

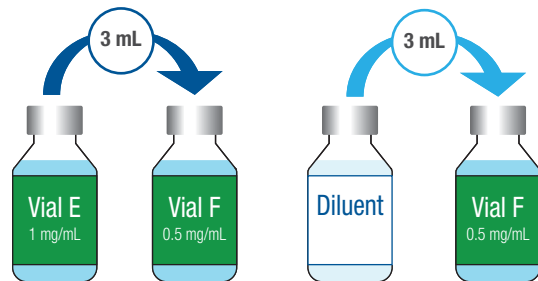
1. Using the Provocholine needle and syringe, draw 3 mL from Vial D (2 mg/mL) and transfer to Vial E.
2. Using the diluent needle and syringe, draw 3 mL of diluent and transfer to Vial E.
3. Shake well.



6 Preparing Vial F

0.5 mg/mL Solution

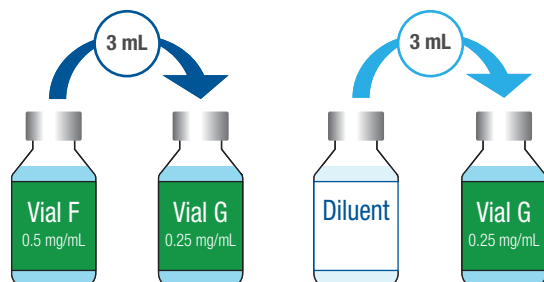
1. Using the Provocholine needle and syringe, draw 3 mL from Vial E (1 mg/mL) and transfer to Vial F.
2. Using the diluent needle and syringe, draw 3 mL of diluent and transfer to Vial F.
3. Shake well.



7 Preparing Vial G

0.25 mg/mL Solution

1. Using the Provocholine needle and syringe, draw 3 mL from Vial F (0.5 mg/mL) and transfer to Vial G.
2. Using the diluent needle and syringe, draw 3 mL of diluent and transfer to Vial G.
3. Shake well.

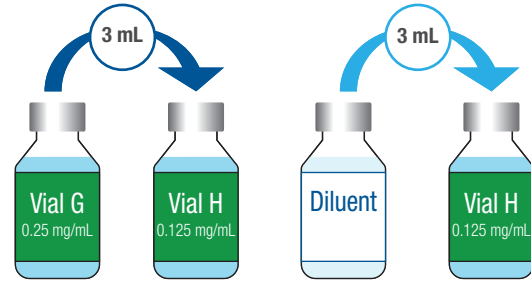


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Preparing Vial H

0.125 mg/mL Solution

1. Using the Provocholine needle and syringe, draw 3 mL from Vial G (0.25 mg/mL) and transfer to Vial H.
2. Using the diluent needle and syringe, draw 3 mL of diluent and transfer to Vial H.
3. Shake well.

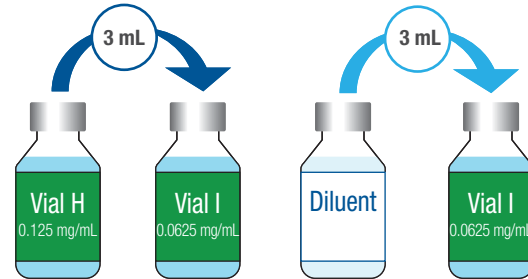


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Preparing Vial I

0.0625 mg/mL Solution

1. Using the Provocholine needle and syringe, draw 3 mL from Vial H (0.125 mg/mL) and transfer to Vial I.
2. Using the diluent needle and syringe, draw 3 mL of diluent and transfer to Vial I.
3. Shake well.

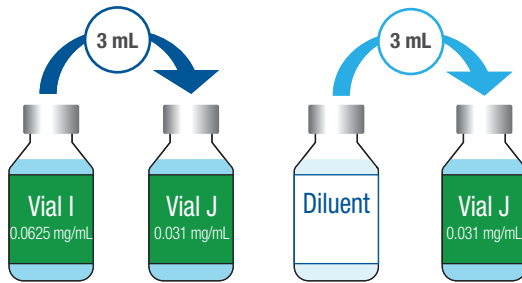


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Preparing Vial J

0.031 mg/mL Solution

1. Using the Provocholine needle and syringe, draw 3 mL from Vial I (0.0625 mg/mL) and transfer to Vial J.
2. Using the diluent needle and syringe, draw 3 mL of diluent and transfer to Vial J.
3. Shake well.



| Vial | Concentration | Final Volume |
|------|---------------|--------------|
| A | 16 mg/mL | 3.25 mL |
| B | 8 mg/mL | 3 mL |
| C | 4 mg/mL | 3 mL |
| D | 2 mg/mL | 3 mL |
| E | 1 mg/mL | 3 mL |
| F | 0.5 mg/mL | 3 mL |
| G | 0.25 mg/mL | 3 mL |
| H | 0.125 mg/mL | 3 mL |
| I | 0.0625 mg/mL | 3 mL |
| J | 0.031 mg/mL | 6 mL |

Storage Instructions

- Provocholine powder should be stored at 15° to 30°C.
- Dilutions (16 mg/mL through 0.031 mg/mL) should be stored at 2° to 8°C in a refrigerator for no more than 2 weeks.
- Be sure to remove the Provocholine dilutions from the refrigerator 30 minutes prior to testing to allow them to warm to room temperature (59° to 77°F or 15° to 25°C as per World Health Organization).

For technical support, please contact us Toll-Free at 1-833-887-7686

®Provocholine (methacholine chloride USP) powder for solution, for inhalation, is marketed in the United States, Canada and other countries. Provocholine is indicated for the diagnosis of bronchial airway hyperreactivity in subjects who do not have clinically apparent asthma. Provocholine is a bronchoconstrictor agent for diagnostic purposes only and should not be used as a therapeutic agent. Provocholine inhalation challenge should be performed only under the supervision of a physician trained in and thoroughly familiar with all aspects of the technique of methacholine challenge, all contraindications, warnings and precautions, and the management of respiratory distress. Emergency equipment and medication should be immediately available to treat acute respiratory distress. For complete prescribing information, please consult the Package Insert which is available for download at www.provocholine.com or on request by calling Methapharm Medical Information at 1-800-287-7686 ext. 7804 or faxing us at 1-877-718-9222. You are encouraged to report negative side effects of prescription drugs to the FDA. Visit MedWatch or call 1-800-FDA(332)-1088. Provocholine is a registered trademark of Methapharm Inc. Copyright © Methapharm Inc. 2017. This information is provided as a professional courtesy, and it is intended to provide data available to us that may assist you in deriving your own conclusions and opinions. This information is not intended to advocate any indications, dosage, or other claim that is not described in the package insert. This dilution sequence was prepared according to the Guidelines for Methacholine and Exercise Challenge Testing, published in 2000 by the American Thoracic Society. This protocol is commonly known as the "ATS Long," and is available for download at <http://www.thoracic.org/statements/resources/piet/methacholine1-21.pdf>.

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Dilution Check Sheet and Control Record

100 mg - Provocholine

ATS "Long" - Doubling Doses

PROVOCHOLINE DILUTIONS FOR CHALLENGE TESTING

Date _____

Prepared by _____

Checked by _____

Provocholine (see vial on label)

Lot Number _____

Expiration Date _____

Diluent _____

Lot Number _____

Expiration Date _____

| Take Provocholine | Add diluent (Shake well!) | Obtain dilution | Vial name | Initial / Date |
|---------------------|------------------------------|-----------------|-----------------------|----------------|
| Provocholine 100 mg | 6.25 mL | 16 mg/mL | Vial A - 16 mg/mL | |
| 3 mL from Vial A | 3 mL | 8 mg/mL | Vial B - 8 mg/mL | |
| 3 mL from Vial B | 3 mL | 4 mg/mL | Vial C - 4 mg/mL | |
| 3 mL from Vial C | 3 mL | 2 mg/mL | Vial D - 2 mg/mL | |
| 3 mL from Vial D | 3 mL | 1 mg/mL | Vial E - 1 mg/mL | |
| 3 mL from Vial E | 3 mL | 0.5 mg/mL | Vial F - 0.5 mg/mL | |
| 3 mL from Vial F | 3 mL | 0.25 mg/mL | Vial G - 0.25 mg/mL | |
| 3 mL from Vial G | 3 mL | 0.125 mg/mL | Vial H - 0.125 mg/mL | |
| 3 mL from Vial H | 3 mL | 0.0625 mg/mL | Vial I - 0.0625 mg/mL | |
| 3 mL from Vial I | 3 mL | 0.031 mg/mL | Vial J - 0.031 mg/mL | |

This set of dilutions will expire on _____