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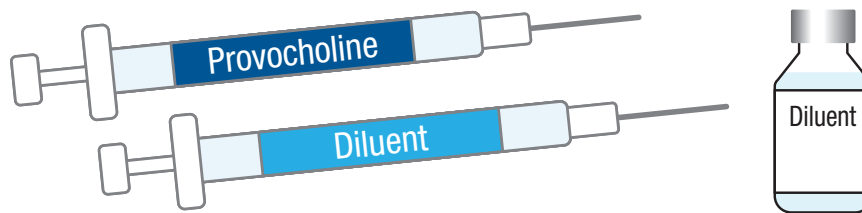
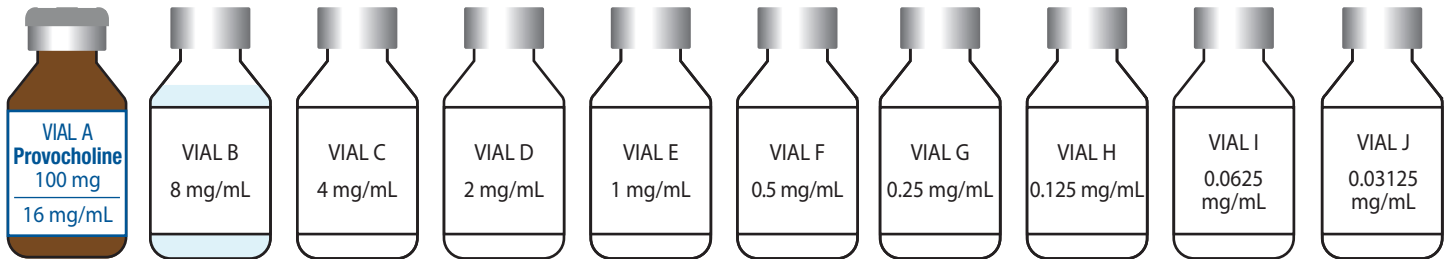
Steps to Diluting Methacholine Chloride ATS “Long” - Doubling Doses



Dilution Sequence Protocol for Provocholine 100 mg/vial (Canada DIN 02239656)

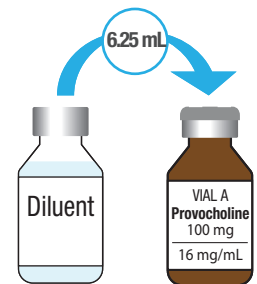
Getting Started

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.



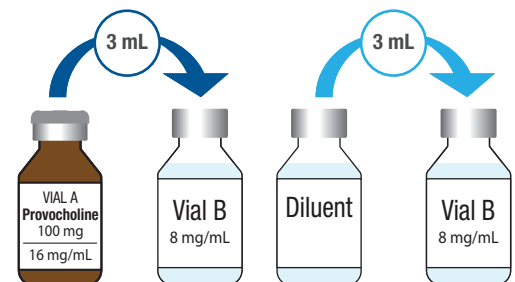
1 Preparing Vial A 16 mg/mL Solution

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

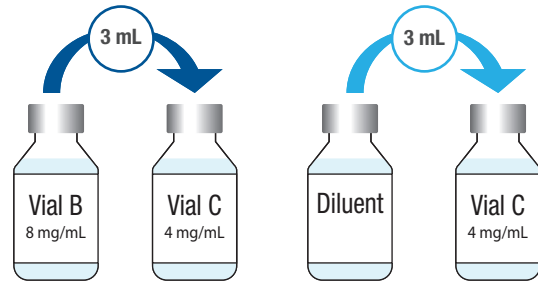
1. Transfer all dilutions (in vials A through E) to nebulizer through the 0.22 µm sterile bacterial retentive filter (Millex GV®).*
2. Be sure to follow your institutional policy for needle and sharps safety.

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

3 Preparing Vial C

4 mg/mL Solution

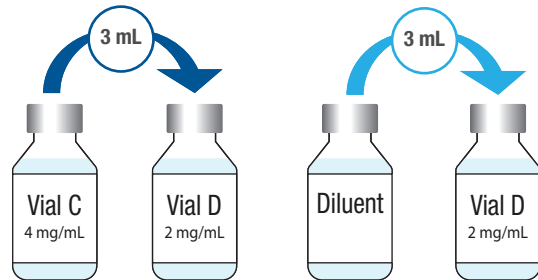
1. Using the Provocholine needle and syringe, draw 3 mL from Vial B (8 mg/mL) and transfer to Vial C.
2. Using the diluent needle and syringe, draw 3 mL of diluent and transfer to Vial C.
3. Shake well.



4 Preparing Vial D

2 mg/mL Solution

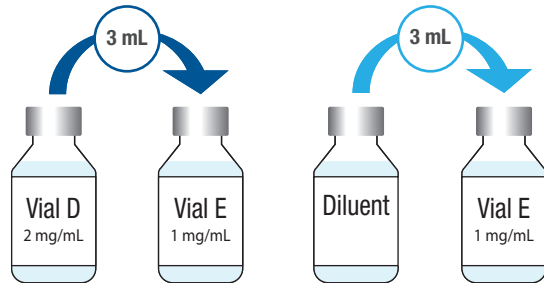
1. Using the Provocholine needle and syringe, draw 3 mL from Vial C (4 mg/mL) and transfer to Vial D.
2. Using the diluent needle and syringe, draw 3 mL of diluent and transfer to Vial D.
3. Shake well.



5 Preparing Vial E

1 mg/mL Solution

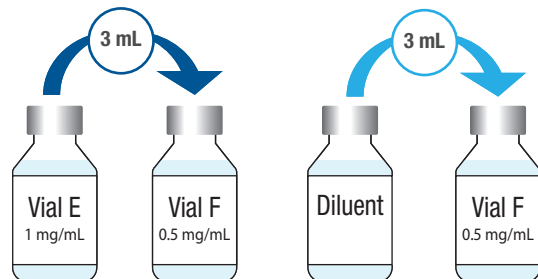
1. Using the Provocholine needle and syringe, draw 3 mL from Vial D (2 mg/mL) and transfer to Vial E.
2. Using the diluent needle and syringe, draw 3 mL of diluent and transfer to Vial E.
3. Shake well.



6 Preparing Vial F

0.5 mg/mL Solution

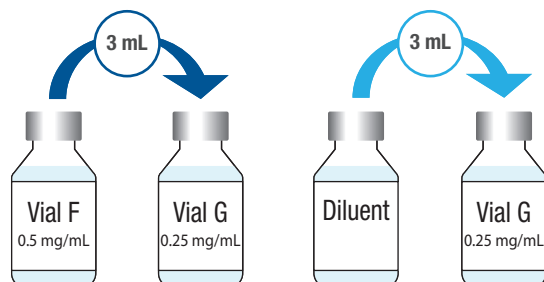
1. Using the Provocholine needle and syringe, draw 3 mL from Vial E (1 mg/mL) and transfer to Vial F.
2. Using the diluent needle and syringe, draw 3 mL of diluent and transfer to Vial F.
3. Shake well.



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.

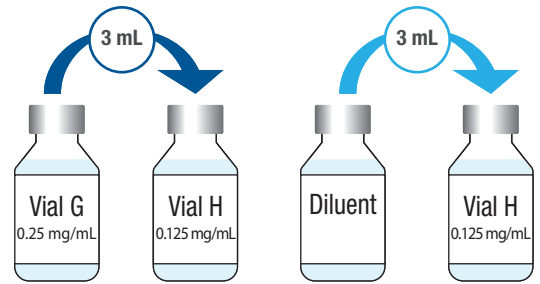


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Preparing Vial H

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.

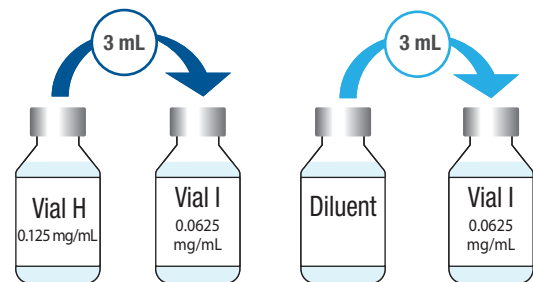


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Preparing Vial I

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.

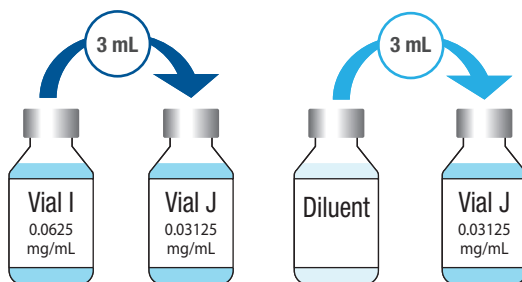


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Preparing Vial J

0.03125 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	0.03125 mg/mL	6 mL

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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.

Storage Instructions

- Provocholine powder should be stored at 59° to 86°F (15° to 30°C).
- Dilutions A through E (16 mg/mL through 0.0625 mg/mL) should be stored at 36° to 46°F (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).

WARNING: SEVERE BRONCHOCONSTRICTION

Severe bronchoconstriction can result from Provocholine administration (including the lowest dose). The use of Provocholine is contraindicated in pediatric and adult patients with baseline FEV₁ <70% predicted or adults with FEV₁ <1.5 L. Because of the potential for severe bronchoconstriction, the use of Provocholine in patients with clinically apparent asthma or wheezing is not recommended [see Warnings and Precautions (7) of the Product Monograph].

Emergency equipment and medication should be immediately available to treat acute respiratory distress. If severe bronchoconstriction occurs, reverse immediately with a rapid-acting inhaled bronchodilator agent (β -agonist) [see Warnings and Precautions (7) of the Product Monograph].

If baseline spirometry is not performed or measured inaccurately, the initial FEV₁ may be underestimated. In this situation, decreases in FEV₁ may not be detected after administration of escalating Provocholine doses, which may result in administration of unnecessary higher doses and an increased risk for excessive bronchoconstriction [see Warnings and Precautions (7) of the Product Monograph].

Please see Product Monograph for full prescribing information, which is available on request by calling Methapharm Medical Information at 1-866-701-4636 or by email: medinfo@methapharm.com. You can report any suspected side effects associated with the use of health products to Health Canada by calling toll-free 1-866-234-2345 or by visiting the web page on Adverse Reaction Reporting (<http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php>) for information on how to report online, by mail or by fax. 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 described in the Product Monograph. For all other inquiries, please call 1-800-287-7686 for Customer Service. This protocol is commonly known as the "ATS Short," and is available for download at <https://www.thoracic.org/statements/resources/pfet/methacholine1-21.pdf>.

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For technical support, please contact us Toll-Free at 1-800-287-7686

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Respiratory

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 _____