alzaid®

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4 packets of polymer beads
One instruction sheet

DURECT™ DURECT Corporation, Cupertino, CA 95014

Chemical Compatibility Test Kit for ALZET® Osmotic Pumps 0004750

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ALZAID® CHEMICAL COMPATIBILITY TEST KIT
INSTRUCTION SHEET

A. General Instructions

The ALZAID® Chemical Compatibility Test kit allows researchers to determine the compatibility of agents and solvents with ALZET® Osmotic Pumps. The Test Kit contains polymer spheres that are chemically identical to the polymer used in the reservoir of ALZET® Osmotic Pumps. The polymer spheres have been processed in the same manner as the drug reservoir, and have been sterilized with gamma irradiation.

The ALZAID® Test Kit can be used to determine the compatibility of a solvent alone, or of agent-solvent solutions, by following the recommended procedures. DURECT strongly recommends the use of this Test Kit when:

1. The solvent you wish to use is NOT on the following list of compatible solvents. (Percentages are weight for weight.)

- Acids, pH greater than 1.8
- Bases, pH less than 14
- Cremophor EL, up to 25% in water
- Culture media (1% benzyl alcohol as bacteriostatic)
- Dextrose, up to 5%, in water or NaCl
- N,N-Dimethyl formamide (DMF), up to 25% in water
- DMSO, up to 50% in water or polyethylene glycol
- DMSO, up to 50%, in ethanol (≤15%) and water
- Ethanol, up to 15% in water*
- Glycerol
- 1-Methyl-2-Pyrrolidone, up to 12.5% in water
- Phosphate buffer
- Polyethylene glycol 300 or 400, neat or in water
- Propylene glycol, neat or in water
- Ringer's solution (with or without lactate)
- Saline, 0.9% (or other aqueous salt solution)
- Serum (rat, mouse, etc.)
- Solutol, up to 30% in water
- Triacetin, up to 5% in water
- Tween 80, up to 2%
- Water, distilled

* Results obtained when using ALZAID® Test Kit with ethanol will not be reliable.

2. The agent is in its free base form.

3. The agent is known to bind tenaciously to polymeric materials.

B. Assessing Solvent Compatibility with ALZET pumps

1. Count and weigh the contents of 1 bag of spheres for each test solution you wish to examine. Record the numbers of spheres and record their weight to the nearest 0.1 mg.

2. Place the weighed group of spheres in a screw-cap test tube (approximately 10 ml in volume).

3. Place 5 ml of the test solvent in the test tube and secure the cap.

4. Incubate the spheres in the test solvent at 37° C for the desired duration of infusion. During the incubation period, the spheres may whiten (this color change is acceptable).

5. Remove all of the polymer spheres from each test tube and blot dry with an absorbent tissue. Immediately count and weigh the group of spheres on an analytical balance to the nearest 0.1 mg. **It is important to finish this step with the same number of spheres with which you began.**

6. For each test solvent, determine the quantity A using the following equation:

$$[(\text{Weight}_{final} - \text{Weight}_{initial}) / \text{Weight}_{initial}] \text{ X } 100 = \text{A } (\%)$$

7. If A is between 0-7%, the solvent is suitable for use with ALZET® Osmotic Pumps. If A is outside of this range (either negative or greater than 7%) or if the spheres deform in shape, the solution should **NOT** be used with ALZET® Osmotic Pumps.

C. Assessing Agent Compatibility with ALZET pumps

1. Using a compatible solvent, prepare a solution of the agent in the concentration which is intended for use in the ALZET® Osmotic Pumps.

2. Place 1 ml of the solution in each of two screw-cap test tubes. Note the clarity of the solution.

3. Place the contents of 1 bag of spheres in one test tube. The other test tube will act as a control. Cap both test tubes.

4. Incubate solutions at 37° C for the desired duration of your ALZET® osmotic pump experiment, e.g., 1 week, 2 weeks, or 4 weeks.

5. At the end of the incubation time, inspect the clarity of the solution in each test tube. Determine the concentration of agent in each.

6. After incubation, the solution in each test tube should have the same clarity as in step 2. If both solutions (test and control) become cloudy, the agent may be unstable. If the solution with polymer spheres becomes cloudy and the control remains unchanged, the agent is unstable in the presence of the polymer spheres. Therefore, this agent should **NOT** be used inside the ALZET® Osmotic Pumps.

7. The concentration of agent in the test tube with polymer spheres should be within 90% of the control value. If not, the agent may be unstable in the formulation at 37° C for the duration of the experiment. The following may have occurred:

   a. the agent is partitioning into the polymer spheres,
   b. the agent is binding to the surface of the polymer spheres,
   c. the polymer spheres are degrading the agent in solution.

If the results of either study indicate problems, please call ALZET® Technical Services at (800) 692-2990 for further assistance and suggestions for alternate approaches.

DURECT has developed a method to deliver an incompatible solvent by displacement from a reservoir (PE 60 catheter tubing) external to the pump reservoir. Please call ALZET® Technical Services for further information on this procedure.

ALZET Technical Information Services
DURECT Corporation
10240 Bubb Road
PO Box 530
Cupertino, CA 95015-0530

800-692-2990 (U.S. and Canada)
408-367-4036 (Outside of the U.S.)
408-865-1406 (Facsimile)
alzet@durect.com (e-mail)
www.alzet.com