Food and Drug Administration
Center for Drug Evaluation and Research

Endocrinologic and Metabolic Drugs Advisory Committee
The Hilton, 8727 Colesville Road, Silver Spring, MD

Discussion Issues
September 25, 2002
Clinical Trials for New Osteoporosis Treatments

Background
In recent years, typical registration dossiers for new drugs for postmenopausal osteoporosis have included trials demonstrating:

1. For treatment, a statistically significant reduction in the incidence of morphometric vertebral fracture vs. placebo over 3 years.

2. For prevention, demonstration of a statistically significant increase in lumbar spine bone mineral density vs. placebo over 2 years, as well as demonstration of anti-fracture efficacy from a treatment trial.

Issue:
Considering the following hypothetical osteoporosis drugs (or others) in development**:**

a. new amino bisphosphonate
b. new estrogen or other agent acting as an estrogen agonist on bone (e.g., SERM)
c. new molecular/mechanistic class antiresorptive agent
d. new bone anabolic agent

To what extent should we modify the standard(s) of clinical evidence required to approve a drug for the prevention and treatment of postmenopausal osteoporosis?

Efficacy:
1. When is bone mineral density an adequate primary endpoint?

2. What duration of study is appropriate for the assessment of effectiveness?

3. When is the use of a placebo or an active control appropriate?

Safety:
1. Can the incidence of osteoporotic fractures be used as a safety rather than an efficacy endpoint?

2. What other specific safety monitoring should be conducted?

3. What duration of study is appropriate for the assessment of safety?

4. When is the use of a placebo or active control appropriate?