

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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SANDOZ INC.,

Petitioner

v.

ELI LILLY AND COMPANY,

Patent Owner

U.S. Patent 7,772,209

Issue Date: Aug. 10, 2010

Title: Antifolate Combination Therapies

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*Inter Partes* Review No. 2016-00318

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**PETITION FOR INTER PARTES REVIEW OF  
U.S. PATENT NO. 7,772,209 PURSUANT TO  
35 U.S.C. §§ 311-319 AND 37 C.F.R. § 42**

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## TABLE OF AUTHORITIES

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