

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

ELI LILLY AND COMPANY,
Petitioner,

v.

TEVA PHARMACEUTICALS INTERNATIONAL GMBH,
Patent Owner.

CASE IPR2018-01710
Patent 8,586,045

PATENT OWNER'S SURREPLY

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I. Introduction

Teva's Patent Owner Response ("POR") exposed multiple infirmities that defeat Lilly's obviousness case. Lilly's principal references—Olesen and Tan—would not have motivated a POSA to treat migraine with anti-CGRP antibodies. Olesen describes a migraine study with BIBN4096BS, which, contrary to Lilly's allegations, cannot be extended beyond small-molecule receptor antagonists. Tan is even further removed from the claimed methods: it is a basic research paper attempting to "prob[e] the role of CGRP as an endogenous vasodilator" in rats, reporting that a full-length anti-CGRP antibody failed to show immunoblockade *in vivo*.

Unable to overcome these and other fatal defects, Lilly instead argues that the claims "do not require clinical efficacy and do not mention safety," and Lilly does not have the burden of showing that "the claimed methods would be clinically effective and safe." Reply, 3. Lilly is wrong. First, the claims must be construed to require therapeutic efficacy. Second, it was Lilly who relied on an alleged "lower toxicity" of humanized antibodies as a reason to combine the art; Lilly cannot now retreat from the relevance of safety considerations on Reply. Teva rebutted Lilly by, *inter alia*, showing that Lilly failed to demonstrate *efficacy* and to fully consider *safety*.

Lilly's hindsight-driven argument selectively cherry-picks references Lilly

believes support its arguments, while ignoring references that undermine them.

Even worse, on cross, Lilly's expert Dr. Charles and his replacement, Dr.

Balthasar¹, distanced themselves from unfavorable portions of Lilly's *own*

references. And they refused to consider teachings that highlight safety concerns associated with long-term inhibition of CGRP.

On Reply, Lilly pivots from its initial rationale, arguing instead that Lilly does not have to consider safety. But Lilly cannot re-craft its challenge to attempt to rehabilitate its Petition. *Henny Penny Corp. v. Frymaster LLC*, No. 18-1596 (Fed. Cir. 2019).

Lilly's new arguments that Covell's carcass studies support its speculation that Tan's antibody would eventually reach its site of action given more time fail, because "***assignment of a site*** ... of antibody localization ***was not possible***."² Similarly, Lilly's speculation about "increased dose" goes against safety concerns regarding long-term CGRP ligand antagonism, which would remove CGRP's protective role during ischemic events, where the risk of stroke and heart attacks are elevated.

¹ On Reply, Lilly proffered testimony from new expert Dr. Balthasar to repair Dr. Charles' discredited opinions. POR, 3-4.

² Emphasis added throughout unless otherwise noted.

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