

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

**HOLOGIC, INC.,
and BECTON, DICKINSON AND COMPANY,
Petitioners**

v.

**ENZO LIFE SCIENCES, INC.
Patent Owner**

**Case No. IPR2016-00822
U.S. Patent No. 7,064,197**

PETITIONERS' REPLY

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I. PRELIMINARY STATEMENT

The Board recognized in its Institution Decision that it is more likely than not that the challenged claims are unpatentable based on the grounds presented in Hologic's Petition. Nothing in Enzo's Patent Owner Response calls that into question. The conclusory and unsupported arguments of Enzo's technical expert, Dr. Gregory Buck ("Buck") fails to alter the Board's reasoning in its Institution Decision. The Board should issue a Final Written Decision canceling the challenged claims.

II. ARGUMENTS

A. Claims anticipated by Fish.

1. Single-stranded (ss) nucleic acids fixed to a non-porous solid support.

The Decision properly concludes that Fish explicitly discloses binding of ssDNA to PLL-coated wells. Decision, 11-12.

The Decision states that Fish "knew that ssDNA would bind to PLL-coated wells, because they were relying on such binding to carry out their experiment." Decision, 12. The Decision quotes the following supporting sentence from Fish: "[t]his positive control for nuclease S₁ activity suggests that single-stranded nucleic acid, bound to PLL treated plastic, remains susceptible to the hydrolytic activity of the enzyme." Ex.1006, 538, right col., ¶1.

Enzo's alternative interpretation of the sentence— Fish *assumed* that ssDNA may have bound—does not make sense. Response, 5. The Decision got it right.

Enzo claims that “additional information” suggests Fish would not have known ssDNA bound. Response, 4-5; Ex.2142, ¶73. Enzo first argues that prior hybridization methods involved ssDNA bound to porous materials or cells bound to nonporous materials. As a consequence, Enzo argues that a POSITA would not expect ssDNA to bind to PLL-coated polyvinyl plates. Response, 4-5; Ex.2142, ¶74. Enzo's alleged state of the art, which did not address PLL binding to nucleic acids, sheds no light on what the Fish authors knew about binding ssDNA to PLL-coated wells.

Enzo oddly asserts that Fish's doubt that DNA would bind to *uncoated* polyvinyl somehow counters the Decision's conclusion that Fish knew ssDNA would bind to *PLL-coated* polyvinyl. Response,4.

Fish proves that dsDNA bound to the PLL-coated wells. Response, 4; Ex.1035, 56:25-57:5. Enzo argues that those dsDNA experiments were unreliable for assessing whether ssDNA would bind in view of unspecified differences between ssDNA and dsDNA. Ex.2142, ¶76. But both ssDNA and dsDNA have negatively-charged backbones, which allow them to bind to positively-charged

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