

# Implementation of the new ASCO/CAP guidelines for *HER2* testing in the clinical laboratory

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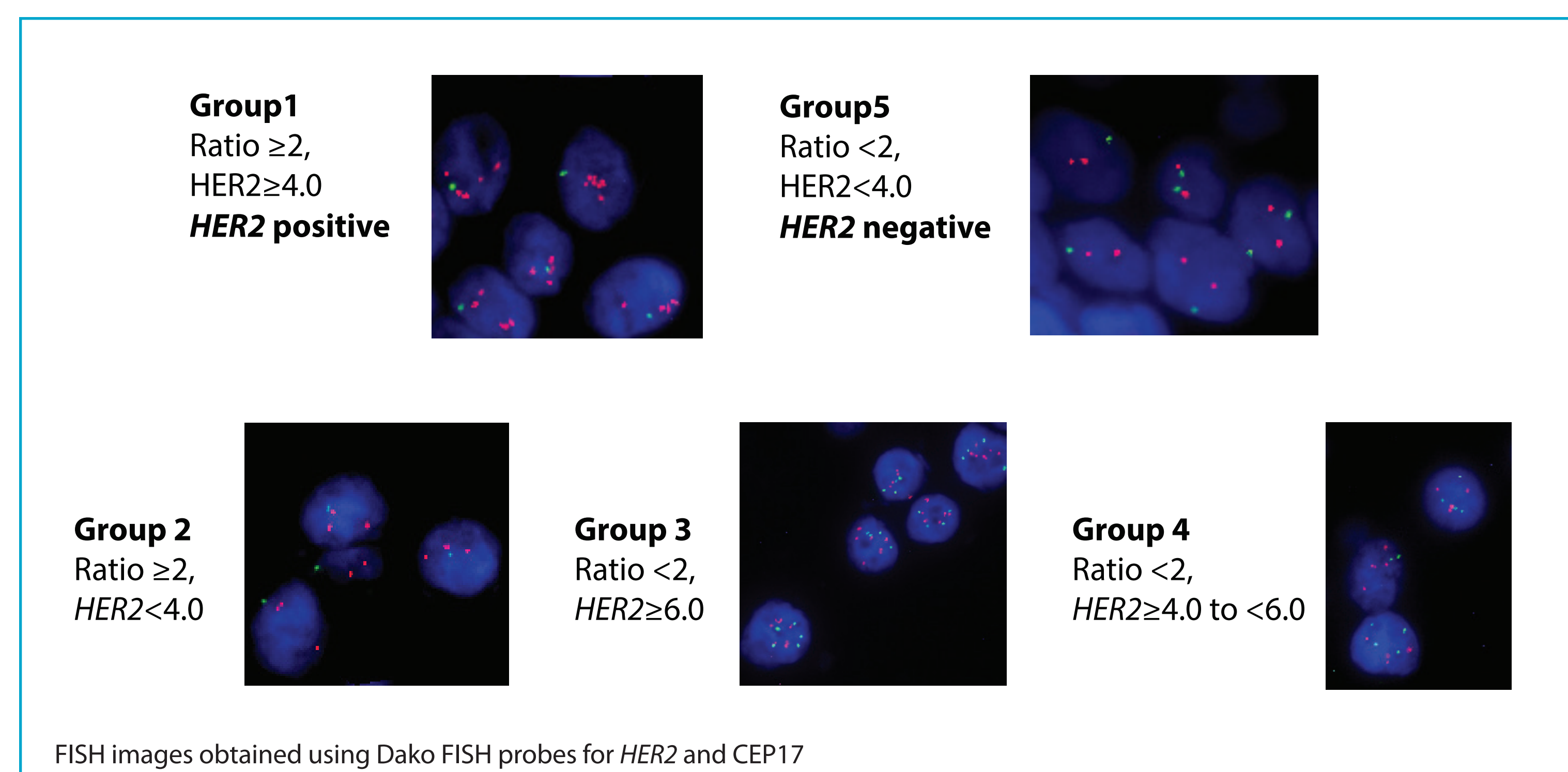
## I. Introduction

Human Epidermal Growth Factor Receptor 2 (*HER2*, *ERBB2*) testing provides important prognostic and predictive information for women with breast cancer. Approximately 4-12% of cases evaluated by FISH have hybridization patterns that are not clearly positive or negative. In 2018, the American Society of Clinical Oncology (ASCO) and College of American Pathologists (CAP) issued updated testing guidelines, which integrate concomitant IHC review for FISH cases with an unclear result (groups 2, 3, and 4), to make a final *HER2* result determination. In this study, implementation of the 2018 ASCO/CAP *HER2* guidelines is presented.

## II. Material and Methods

A total of 776 specimens (479 ordered for IHC with reflex to FISH and 297 ordered for FISH only) were tested since implementing the new guidelines. All cases were processed in accordance with the new 2018 ASCO/CAP testing guidelines. For samples with a *HER2* result of groups 2-4, concomitant review of IHC from the same block used for FISH was used to guide a final *HER2* result determination.

### Example *HER2* FISH Result Categories and Workflow



### IHC needed

- Groups 2, 3, and 4 require pathologist review of IHC to identify areas of potential *HER2* amplification.
- LabCorp informs the physician that per 2018 guidelines *combined FISH and IHC* is required to determine *HER2* result status.
- If IHC is performed by an outside lab, the slide may be reviewed for the sole purpose to guide the group 2-4 FISH analysis. No IHC report is provided.

### IHC 0, 1+, or 3+

- If IHC is 0 or 1+ then the diagnosis is *HER2* negative with a comment.
- If IHC is 3+ then the diagnosis is *HER2* positive.

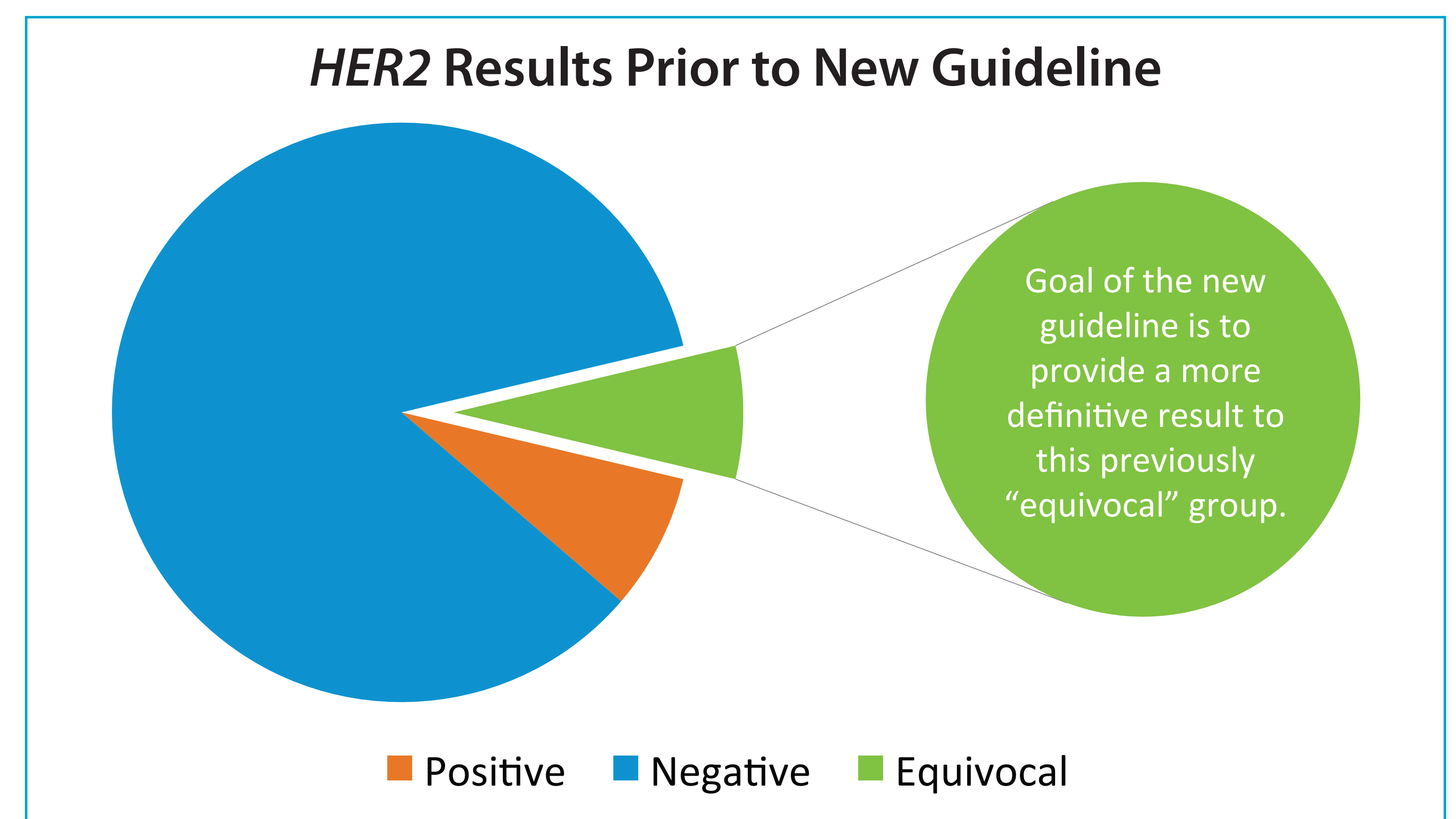
### IHC 2+

- FISH reports group 1 positive, group 5 negative and groups 2-4 reflex to IHC
- Pathologist circles area of weak to moderate complete membrane IHC stained region and reflexes to FISH.
- Additional 40 cells are analyzed and groups are assigned.
- If the subsequent FISH analysis agrees with the initial analysis; **2=negative; 3=positive; 4=negative with comment.** Adjudication is required if the first and second groups differ.
- Final adjudicated category assigned based on greatest concordance – closeness of two of three analysts and FISH is reported as FISH negative or positive.

## III. Results

A total of 2,488 specimens tested for *HER2* prior to implementation of the new guidelines were examined.

Prior to the guidelines, 7.4% of cases ordered for *HER2* testing were reported with equivocal results (7.6% were positive, 85% were negative).

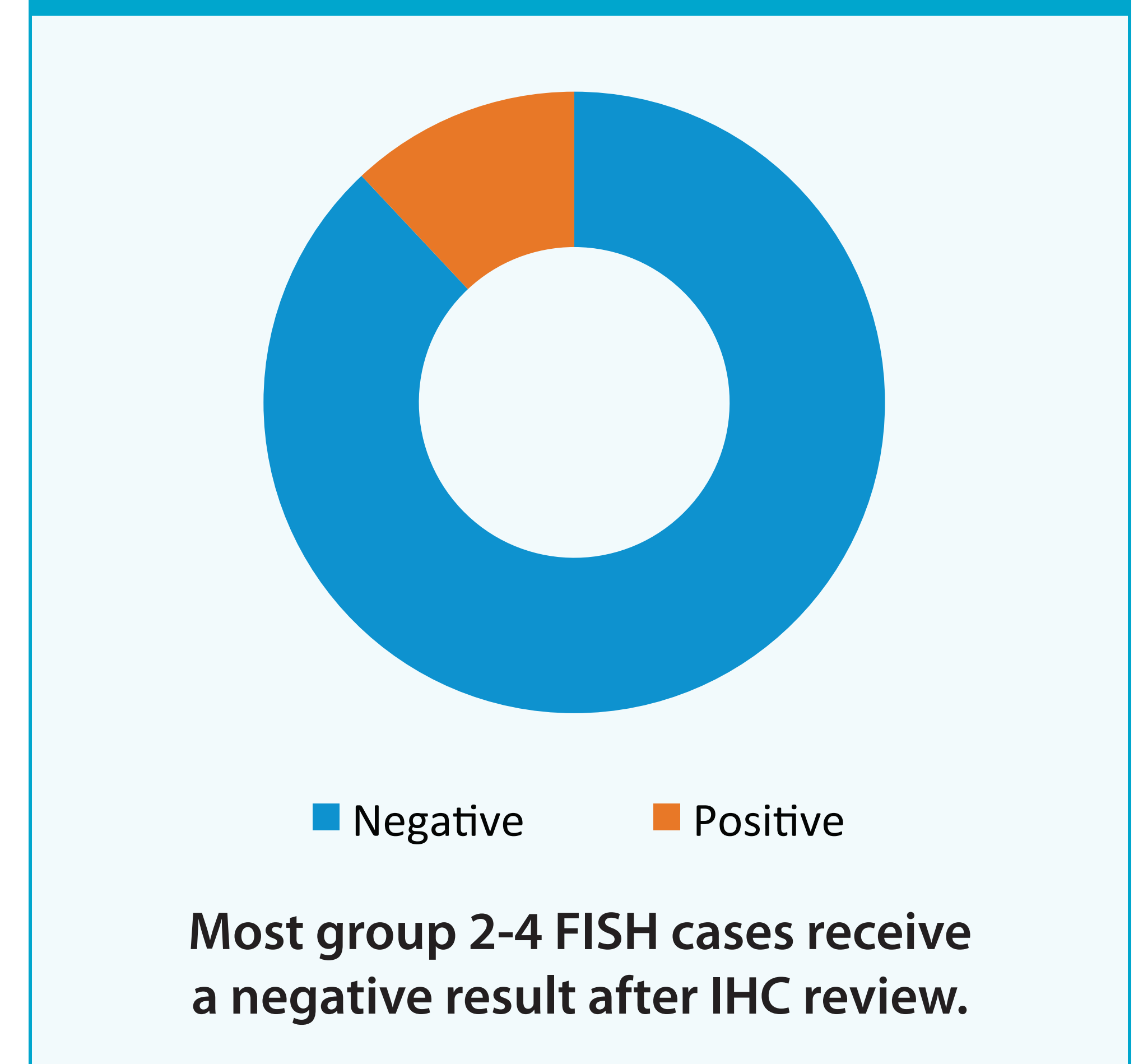


After implementation of the guidelines, 11.1% fell into groups 2-4.

After concomitant review of the IHC from the same block used for FISH, 88% received a final result of negative.

A total of 12% received a final result of positive, including two group 4's, where IHC 2+ was received from an outside laboratory that became positive after internal IHC review.

### Final *HER2* Results After IHC Review of Group 2-4 FISH Cases



## IV. Conclusion

Adaptation of the guideline resulted in an increase in the number of negative results, but importantly identified some patients as positive.

Additional training was required for both laboratory personnel and customer service representatives to streamline interactions with IHC/pathologists and handle inquiries from clients regarding the new guidelines.

This study illustrates the importance of implementing the new guidelines so patients will receive a definitive result, and clinicians can make informed therapeutic decisions.

## V. Reference

Wolff AC, et al. Human Epidermal Growth Factor Receptor 2 Testing in Breast Cancer: American Society of Clinical Oncology/College of American Pathologists Clinical Practice Guideline Focused Update. *J Clin Oncol*. 2018 Jul10; 36(20):2105-2122. PMID: 29846122.