IN THE SUPREME COURT OF THE STATE OF HAWAI'I

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STATE OF HAWAI'I, EX REL. HOLLY T. SHIKADA, ATTORNEY GENERAL,
Plaintiff-Appellee,

vs.

BRISTOL-MYERS SQUIBB COMPANY; SANOFI-AVENTIS U.S. LLC;
SANOFI US SERVICES INC., formerly known as
SANOFI-AVENTIS U.S. INC.; and SANOFI-SYNTHELABO LLC,
Defendants-Appellants,

and

SANOFI S.A., Defendant-Appellee.

SCAP-21-0000363

CERTIORARI TO THE INTERMEDIATE COURT OF APPEALS
(CAAP-21-0000363; CASE NO. 1CC141000708)

MARCH 15, 2023

RECKTENWALD, C.J., NAKAYAMA, McKENNA, AND EDDINS, JJ.;
AND WILSON, J., DISSENTING[1]

OPINION OF THE COURT BY EDDINS, J.

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[1] At the time of this opinion's publication, Justice Wilson's dissent is forthcoming.

I. INTRODUCTION

This case is about whether two pharmaceutical companies — Defendants-Appellants Bristol-Myers Squibb and Sanofi — violated Hawaiʻi's Unfair or Deceptive Acts or Practices law (UDAP) by misleading the public about the safety and efficacy of their antiplatelet drug, Plavix.

The State, in a 2014 complaint, alleged that Plavix was less effective in patients who had certain liver-enzyme mutations (poor responders). It said that people with these mutations had worse outcomes on Plavix than others, and that Defendants knew this fact years before 2009, when the FDA updated Plavix's label with information about the poor responder issue.

The State alleged Defendants violated Hawaiʻi law in two ways. First, it asserted that the companies – despite knowing about the issues with Plavix – failed to update the drug's warnings to inform the public. Second, the State claimed the defendant companies intentionally kept the poor responder issue under wraps and suppressed research into it in order to protect their bottom line.

The Circuit Court of the First Circuit agreed with the State on both points. After a bench trial that spanned more than a month, the court held that Bristol-Myers Squibb and

Sanofi had violated UDAP by engaging in deceptive and unfair acts and practices.

The court said the defendant companies misled Hawaiʻi consumers by failing to warn them that Plavix was less effective for poor responders. It found that this omission injured consumers by denying them the drug's full promised antiplatelet effect, hindering their ability to give informed consent, and preventing them from taking an alternative drug or undergoing genetic testing to determine whether they were poor responders. The court also faulted Defendants for both refusing to adequately research variability of response and suppressing research that might confirm a link between ethnicity or genotype and Plavix responsiveness.

For these acts, the court imposed an $834 million penalty.

We vacate this penalty.

The court improperly granted the State's motion for partial summary judgment on a central trial issue: Did the label matter to consumers?

The summary judgment ruling on materiality circumscribed the companies' ability to present a full defense, marred the court's deceptive acts holding, and affected the penalty award. Bristol-Myers Squibb and Sanofi are entitled to a new trial on the deceptive acts or practices claim.

But there will be no second trial on the unfair acts or practices claim. The court's holding that the companies committed unfair acts under UDAP has sufficient, independent evidentiary support.

We also conclude that Defendants' procedural arguments fail. The court correctly determined that the State's claims were not barred by UDAP's safe harbor provision or its statute of limitations. Nor were they preempted by federal law.

We (1) reverse and remand the court's deceptive acts UDAP holding, (2) vacate the court's grant of partial summary judgment and the penalty award, (3) affirm the court's unfair acts UDAP holding, and (4) remand for a penalty award after the deceptive-acts claim is resolved.

II. BACKGROUND

A. Factual Background

Defendants-Appellants Bristol-Myers Squibb and Sanofi[2] are multinational pharmaceutical companies that developed Plavix, an antiplatelet or "blood thinner" drug.

Platelets, tiny pieces of cells in the bloodstream, can form clots which create serious health problems like heart attacks. Doctors often prescribe Plavix along with aspirin (called dual anti-platelet therapy or DAPT) to patients with

[2] The defendant companies are Bristol-Myers Squibb Company (BMS) and Sanofi-Aventis U.S. LLC, Sanofi US Services Inc., formerly known as Sanofi-Aventis U.S. Inc., and Sanofi-Synthelabo LLC (Sanofi).

heart problems or patients who have recently had a procedure that might put them at risk for platelet clotting, such as angioplasty[3] or cardiac stenting.

Cardiac stents work by propping and holding open arteries to improve blood flow. Stents can disturb the plaque naturally lining our arteries. Platelets in the blood can then accumulate around the disruption, forming a clot. Patients may take blood thinners like Plavix to inhibit this clot formation.

Plavix's chemical name is "clopidogrel." Clopidogrel is a "prodrug," meaning it is only effective once it is changed by the body. Plavix achieves its antiplatelet effect when it is metabolized by the liver.

There are a family of enzymes in the liver, called the "Cytochromes P450" (CYP) that are commonly involved in metabolizing prodrugs.

Several CYP450 liver enzymes are involved in metabolizing Plavix. The liver enzyme CYP2C19 is one of them.

Different factors affect how well someone can metabolize Plavix. "Variability of Response" is "a blanket term that basically reflects that no one person responds the same to any pharmaceutical agent." There will be variability of response to

[3] Angioplasty is a medical procedure for opening clogged or narrow arteries. It involves inserting a small catheter with a balloon tip into a blood vessel, and it can also be used to place stents in arteries. Coronary angioplasty and stents. https://www.mayoclinic.org/tests-procedures/coronary-angioplasty/about/pac-20384761 [https://perma.cc/B6SX-NM68].

all drugs. And it can be caused by intrinsic factors like height, weight, sex, and genetics, or by extrinsic factors like smoking, diet, exercise, and other drugs a patient is taking.

If a prodrug is metabolized by CYP2C19, then genetic variation in the CYP2C19 liver enzyme can cause "poor responsiveness" to that drug.

Pharmacogeneticists use the star allele system to describe genetic variation in liver enzymes.

The *1 genetic version of CYP2C19 (CYP2C19*1) confers fully functional CYP2C19 enzymes. The other versions of CYP2C19 (CYP2C19*2, *3, *4, *5, *6, *7, or *8) confer a reduced ability to metabolize Plavix. The CYP2C19*2 and CYP2C19*3 genetic types are the most commonly linked to poor Plavix responsiveness.

Each person has two CYP2C19 alleles.

People with two CYP2C19*1 alleles will have a CYP2C19 liver enzyme that is very good at metabolizing Plavix; those with one CYP2C19*1 and one CYP2C19*2 or *3 allele will be "intermediate metabolizers" and someone with two CYP2C19*2 or CYP2C19*3 alleles (or one *2 and one *3) will be a "poor responder."

Scientific understandings of CYP2C19's role in metabolizing Plavix have evolved over time.

When Plavix launched in the late 1990s, it was known that the CYP450 enzymes — of which CYP2C19 is one — were involved in metabolizing Plavix. But the extent of the enzyme's role in

metabolizing Plavix and – by extension — the possibility that poor responders might get less benefit from the drug — were not generally known at that time.

Terms like "poor responder" or "Plavix resistant" are used (sometimes interchangeably) to refer to two distinct things: (1) the genetic makeup of a person's CYP2C19 enzymes; and (2) the ability of a person's liver enzymes (either collectively or isolated CYP2C19 enzymes alone) to metabolize Plavix in a test tube (called platelet-function).

There is consensus that a genetic "poor responder" is someone with two *2 or *3 alleles. But there is less consensus about what level of response to Plavix (either in a test tube or in the real world) makes someone a "poor responder" from a platelet-function perspective.[4]

CYP2C19 is not the only enzyme involved in Plavix's metabolization. And factors other than CYP2C19 genotype impact the likelihood of adverse clinical outcomes, including blood vessel size, family history, and lifestyle factors like diet or smoking.

[4] The trial court collectively called those patients that had less than 20% response to the drug or those with zero response to the drug "poor responders." The court's classification of "poor responders" matched the companies' rubric, which used a cut off of 20% for their meta-analysis. But a pharmacogenetics team leader for BMS pointed out that the 20% response line was "a somewhat arbitrary distinction," because it was "not based on clinical outcomes" of the patients. She added, "what's the difference between 20 percent from the mean or 25 percent from the mean? It's an author's choice."

B. Procedural Background

This lawsuit began in March 2014 when the State filed a complaint alleging Bristol-Myers Squibb and Sanofi violated Hawaiʻi's Unfair or Deceptive Acts or Practices law.

Under UDAP, "unfair or deceptive acts or practices in the conduct of any trade or commerce are unlawful." HRS § 480-2(a) (2008). The State's complaint alleged that between 1998 and 2010 Defendants had violated this law by: (1) failing to disclose that Plavix has diminished or no effect in poor metabolizers; and (2) allowing their research decisions to be driven by profit-seeking. The State claimed the Defendants' behavior was both deceptive and unfair.

1. Motion for Summary Judgment

The State moved for partial summary judgment on its deceptive acts or practices UDAP allegation.

The State's motion focused on one part of its deceptive acts claim. A deceptive act is defined as: "(1) a representation, omission, or practice that (2) is likely to mislead consumers acting reasonably under the circumstances where (3) the representation, omission, or practice is material." Courbat v. Dahana Ranch, Inc., 111 Hawaiʻi 254, 262, 141 P.3d 427, 435 (2006) (cleaned up). The State argued that the third part – materiality – should not be up for debate.

The State argued that there was no need for a trial to determine the materiality of information about Plavix's lower efficacy for poor responders. There was "no doubt that the information contained in Plavix's federally mandated black box warning is material as a matter of law." Thus, the State asked the court to decide materiality before trial, at summary judgment – it would "eliminate any unnecessary time at trial."

The court resolved the materiality element in the State's favor. It decided that there was no genuine dispute of material fact that Defendants' omission involved "information that is important to consumers and, hence, likely to affect their choice of, or conduct regarding, a product." Courbat, 111 Hawaiʻi at 262, 141 P.3d at 435 (cleaned up).

The court also gave what the companies dubbed an "alternative holding." Since it would fact-find and apply those facts to the law at a bench trial, the court - calling itself the "Ultimate Trier of Fact" - felt it "need not resolve inferences in favor of the non-moving party." It found the defendant companies' evidence "weak and unpersuasive." Materiality, an elemental fact to a deceptive acts UDAP violation, would go untested at trial.

The court's summary judgment ruling precluded Bristol-Myers Squibb and Sanofi from presenting trial evidence about the materiality of the warning. This included evidence showing that

Hawaiʻi doctors and patients hadn't changed how they prescribed or consumed Plavix after information about the poor responder issue was added in 2010 to the black box warning. The court forbade the defendant companies from introducing evidence about what any person "did or did not do in response to, or as a result of, [t]he addition to the Black Box Warning to the Plavix label in 2010."

The rest of the State's case proceeded to trial in October and November, 2020.

2. Trial[5]

The bench trial was a battle royale of testifying pharmacology experts, regulatory experts, and medical doctors. The parties presented evidence on everything from the minutiae of FDA regulations to whether St. John's Wort could enhance Plavix's efficacy.

Much of the trial's myriad and diverse evidence, however, speaks to three central issues.

First, did the defendant companies mislead anyone through omitting the poor responder information from the Plavix label between 1998 and May 2009? Or were the companies just doing the best they could with incomplete and conflicting scientific information about the causes of variability of response to Plavix?

[5] The Honorable Dean E. Ochiai presided.

Second, did Defendants suppress research into variability of response for financial reasons? Did greed prevent them from confirming CYP2C19's role in metabolizing Plavix sooner?

And third, did the omission of the poor responder information from Plavix's label hurt Hawai'i consumers? Did this omission hinder consumers' ability to give informed consent? Were patients duped into taking a drug that might harm them - or at least not help them - because of Defendants' omissions?

a. Deception through omission?

Regarding the first question of whether Defendants deceived consumers though omission, the parties introduced three major categories of evidence at trial: (1) scientific understanding before Plavix launched in 1998, (2) evidence concerning the scientific community's changing perspectives between 1998 and 2010 on which liver enzymes were principally responsible for metabolizing clopidogrel, and (3) evidence concerning shifts in scientific thinking about the link between CYP2C19 genotypes and clinical outcomes after 2010.

i. Pre-approval

Almost four years before the FDA approved Plavix, Dr. Sonia de Morais identified the genetic mutation that causes poor responsiveness in CYP2C19. She looked at the metabolization of S-mephenytoin - a drug that was known to almost exclusively be metabolized by CYP2C19 – not clopidogrel.

Dr. de Morais' 1994 article also introduced the idea of genetic testing for poor response in CYP2C19.[6] For her work, she developed a "simple PCR-based genetic test for [identifying] the defective CYP2C19 allele." She later clarified that by "simple," she meant when "compared to the expensive and laborious technique of complete gene sequencing." Her test "was only focused on the simple small fragment of DNA that had the mutation"; it was not intended for direct patient use.

In addition to identifying (for the first time) CYP2C19*2 and CYP2C19*3, Dr. de Morais' 1994 study found that "[t]here are large interracial differences in the frequency of the poor metabolizer phenotype with [Asian] populations having a five fold greater frequency compared to Caucasians."

Then in 1996, BMS and Sanofi sponsored CAPRIE (Clopidogrel versus Aspirin in Patients at Risk of Ischemic Events): a 19,000-person clinical trial designed to compare the relative efficacy of clopidogrel and aspirin in "reducing the risk of a composite outcome cluster of ischaemic stroke, myocardial infarction, or vascular death." CAPRIE showed that, compared to aspirin, Plavix conferred a "statistically significant

[6] At trial, the State argued that Dr. de Morais' mid-90s genetic test could have been used to research any correlation between CYP2C19 gene mutations and poor response to Plavix early in the drug's development. But it was also clear that easy access to genetic testing for *patients* who could be poor responders has only become available since the boxed warning was added.

reduction" in the risk of death for patients who had recently had a heart attack or stroke or who had peripheral artery disease.

CAPRIE also found a statistically significant relationship between race and treatment outcomes when Whites and non-Whites were compared. The CAPRIE investigators noted, however, that these results should be interpreted cautiously since only 5% of the study population was non-White. Also, non-Whites were not well represented in the peripheral artery disease study group (the subgroup for which Plavix was most effective).

In 1997, BMS and Sanofi investigated which liver enzymes were involved in Plavix metabolization. That study showed that the liver enzymes "CYP2B6, CYP2C19 and CYP3A4 are involved in clopidogrel metabolism in human liver microsomes." It also "suggest[ed] possible involvement of CYP1A2, CYP2C9 and CYP2E1 in clopidogrel metabolism."

On March 5, 1997 – before Plavix's approval — the companies wrote to the FDA proposing a label that stated in relevant part: "In vitro, the isoenzymes responsible for metabolism of clopidogrel and the carboxylic acid derivative are CYP2B6, CYP2C19 and CYP3A4; evidence also suggests possible involvement of CYP1A2, CYP2C9 and CYP2E1 in clopidogrel metabolism." (Emphasis added.)

The FDA prevented Defendants from including that language on the label.

The FDA approved Plavix in November 1997. In its approval letter, the FDA warned Defendants that Plavix's final printed label "must be identical to the enclosed draft labeling" because "[m]arketing the product with [a label] that is not identical to this draft labeling may render the product misbranded and an unapproved new drug."

ii. Post-approval

After Plavix was approved, Defendants conducted a "meta-analysis" of their internal clinical trial data from Phase I and Phase II clinical studies in March of 1998. The meta-analysis was a retrospective review of prior studies that examined previously available data.

The meta-analysis showed there was a variability of response to Plavix. From the 469 samples examined, 67.8% of patients were considered good responders: the drug was at least 20% effective at inhibiting clot formation. Only 3.4% of patients had no response. The extent of that variability depended on the test used to measure inhibition: one test showed that 32.2% of patients had less than 20% platelet inhibition while other tests showed 8.5% of patients.[7]

[7] At trial, the companies' witness explained that the 32.2% value encompassed the patients who had tested at least once for less than 20%

Defendants did not submit the 1998 meta-analysis to the FDA until 2005, seven years after Plavix's launch.[8] When they eventually submitted the meta-analysis to the FDA, it was presented as an appendix to another document.

Just before Plavix reached the market in December, Sanofi released a study in November 1998 which concluded that 57% of clopidogrel metabolization was attributable to the liver enzyme CYP3A4, while 13% was attributable to CYP2C19.[9]

The companies theorized that Plavix might principally be metabolized by CYP3A4. CYP3A4 is "the most abundant" enzyme in the liver, and it has the ability to metabolize a variety of structures. It does not have a loss-of-function allele. CYP3A4 variations are caused by non-genetic factors like diet and interactions with other drugs.

Plavix sales began in December 1998.

(1) 1998-2008

From 1998 to 2008, the defendant companies sponsored various studies on Plavix. Researchers not affiliated with the companies also published on clopidogrel.

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inhibition of platelet aggregation. Of that 32.2%, though, 23% of patients still had an overall inhibition of platelet aggregation over 20%.

[8] Defendants submitted the meta-analysis to Swiss medical authorities shortly after its completion in March 1998; the Swiss required the meta-analysis before they would approve Plavix.

[9] The remaining 30% was attributable to CYP1A2 (18%) and CYP2B6 (12%).

BMS and Sanofi sponsored a large clinical trial, CURE, beginning in 1998 and ending in 2000. CURE found that Plavix plus aspirin reduced the risk of cardiovascular death, heart attack, or stroke by 20% more than aspirin plus a placebo did. Of the 12,562 patients enrolled in the CURE trial, 82.1% (10,308) of them were Caucasian and 2% (254) of them were Asian.

A 2003 study published by researchers outside the companies examined CYP liver enzymes and clopidogrel metabolization. The results showed that CYP3A4 and CYP3A5 did the best job metabolizing clopidogrel.

In June 2003, a BMS research group published an article on clopidogrel. The group was led by Dr. Paul Gurbel - an expert on platelet variability of response, then a BMS scientist, and now a qui tam relator suing the companies elsewhere as he testified for the State at trial. The article described clopidogrel non-responsiveness in 31% of the patient population after procedures such as stenting or angioplasty. The study did not show a correlation between non-responsiveness to Plavix and adverse clinical outcomes.[10] But it did show that Plavix didn't work so well for nearly one in three patients that had stents placed or underwent angioplasty.

[10] Dr. Gurbel's paper implied a connection between clots blocking stents (stent thrombosis) and clopidogrel resistance. But because the rate of stent thrombosis was much lower than the rate of Plavix resistance, the study noted that the two were possibly unrelated.

The defendant companies sponsored the COMMIT study after CURE. COMMIT was a clinical trial in China with more than 45,000 patients; all enrolled patients were Chinese. The results published in 2005 showed that when patients who'd had a heart attack were given Plavix and aspirin, their risk of having an adverse cardiac event dropped by 9%.[11]

Next, the defendant companies sponsored the CHARISMA trial. It was a large scale (15,000-patient) clinical trial comparing Plavix's effects to those of a placebo. It found that *for high-risk patients*, "clopidogrel plus aspirin was not significantly more effective than aspirin alone in reducing the rate of myocardial infarction, stroke, or death from cardiovascular causes."

But, data from the CHARISMA study (published in 2006) showed that Asian patients had the lowest occurrence of death, heart attack, or stroke while taking Plavix.

The shift in focus to CYP2C19 and clopidogrel came in 2006. An independent pharmacogenetics researcher, Dr. Jean-Sebastien Hulot, published a proof-of-concept study which suggested that

[11] After the COMMIT study, the FDA approved a new indication for Plavix: it allowed the drug's prescription to patients who'd had serious heart attacks even if they were not going to have stents put in.

CYP2C19 genetic polymorphism was linked to reduced clopidogrel responsiveness.[12]

Then in October 2008, a study came out examining drug interactions between Plavix and Omeprazole. Omeprazole is a proton pump inhibitor – a type of drug known to impede CYP2C19's function. The study showed that patients prescribed both Plavix and Omeprazole were more likely to have diagnostic codes for things like heart attack and stroke than those who weren't prescribed Omeprazole. Defendants submitted this study to the FDA "outside of the normal annual cycle of reporting."

Defendants met with the FDA. An undated document titled "Response to FDA Discussion Held 05 December 2008" prepared by Sanofi summarized the meeting:

> The discussion centered on whether differences in the formation of the active metabolite could be a primary source of platelet response variability. It was recognized that the relationship between the variability in platelet response and clinical outcome, as well as the intrinsic and extrinsic factors which modulate the formation of the active metabolite, are not well understood. A specific focus of the discussion was the extrinsic [proton pump inhibitor drugs] and intrinsic (genetic polymorphisms) factors which impact the formation of the active metabolite through CYP2C19.

At the December 5, 2008 meeting the FDA asked Defendants to prepare a written action plan "in response to the issues raised." Defendants did. They proposed looking at "drug-drug

[12] Dr. Hulot wrote that "The CYP2C19*2 loss-of-function allele is associated with a marked decrease in platelet responsiveness to clopidogrel in young, healthy male volunteers and may therefore be an important genetic contributor to clopidogrel resistance in the clinical setting."

interaction with proton pump inhibitors" and "genetic polymorphisms and of CYP2C19 and its impact."

(2) 2008-2009

Then on December 22, 2008, Dr. Jessica Mega published the results of a genetic study she had conducted using data collected as part of the TRITON trial. It involved "a head-to-head-comparison" of Plavix and Effient (prasugrel), another antiplatelet that was then under development by Defendants' competitor, Eli Lilly. Dr. Mega's study (the Mega study) showed that clopidogrel-treated patients who carried a loss-of-function allele "had a three-fold greater risk of clotting their stent, and a 50 percent greater risk of having a heart attack, a stroke or death."

The Mega study's results catalyzed discussions between the FDA and Defendants about revising Plavix's label to include information about CYP2C19. The FDA pushed the companies to act. It welcomed a counterproposal from the companies, with the understanding it would disregard unsatisfactory suggestions.

In discussing these revisions, a BMS employee wrote in a March 30, 2009 email to his colleagues:[13]

[13] The court overruled the defendant companies' hearsay objection. The email was not offered for the truth of the matter asserted, the court ruled. Rather, it was evidence of the companies' knowledge and how the Defendants reacted (or not) to the experts' comments. We agree. The evidence was admissible for non-hearsay purposes.

> Problem is that I don't really see a counterproposal but instead it looks like we are into stalling some more. I have to tell you that I have had in depth 1:1's with about 6 senior [key opinion leaders] since I have been at [the American College of Cardiology] and the mood is very negative towards us (people like Dr. Topol, Gurbel, Eikelboom, Fox are all saying that they have been telling us this for years and we chose to ignore them and bury our head in the sand and so they feel no sympathy toward our current situation!)

In May 2009, the FDA amended the "Precautions" section of Plavix's label to read:

> Based on literature data, patients with genetically reduced CYP2C19 function have lower systemic exposure to the active metabolite of clopidogrel and diminished antiplatelet responses, and generally exhibit higher cardiovascular event rates following myocardial infarction than do patients with normal CYP2C19 function (see **CLINICAL PHARMACOLOGY: Pharmacogenetics**).[14]

(First emphasis added.)

The May 2009 label also stated that "patients with an impaired metabolizer status (intermediate and poor combined) had a higher rate of cardiovascular events (death, myocardial infarction, and stroke) or stent thrombosis compared to extensive metabolizers."

Regarding genetic testing, the 2009 label explained that "[p]harmacogenetic testing can identify genotypes associated with variability in CYP2C19 activity."

(3) 2009-2010

Following the May 2009 label update, Defendants and the FDA discussed whether the information should be put in a black box

[14] The May 2009 version of the "Pharmogenetics" section stated: "diminished antiplatelet responses to clopidogrel have been described . . . in 21 reported studies," and that "[t]he relative difference in antiplatelet response between genotype groups . . . is typically greater than 30%."

warning — the most prominent type of warning on a drug label.

The defendant companies told the FDA that Plavix's "labeling adequately describes the safety and efficacy of clopidogrel and that a boxed warning [was] not necessary at this time."

Ultimately, the FDA decided to put the CYP2C19 information in a black box warning in 2010. Like the May 2009 label, the black box included language stating that poor metabolizers taking Plavix are more likely to have adverse cardiac events on the drug than non-poor responders.[15]

iii. After the 2010 Black Box Label

In the first half of the 2010s, several research articles called into question the link between CYP2C19 genotype and clinical outcomes identified by the December 2008 Mega study.[16,17]

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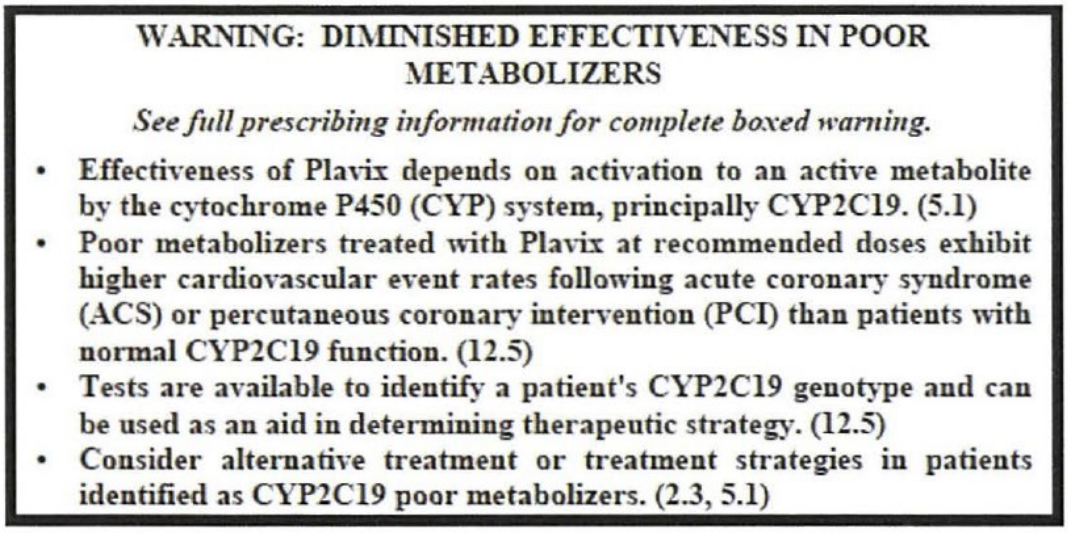
[15] The 2010 Black Box label:



WARNING: DIMINISHED EFFECTIVENESS IN POOR METABOLIZERS

See full prescribing information for complete boxed warning.

- **Effectiveness of Plavix depends on activation to an active metabolite by the cytochrome P450 (CYP) system, principally CYP2C19. (5.1)**
- **Poor metabolizers treated with Plavix at recommended doses exhibit higher cardiovascular event rates following acute coronary syndrome (ACS) or percutaneous coronary intervention (PCI) than patients with normal CYP2C19 function. (12.5)**
- **Tests are available to identify a patient's CYP2C19 genotype and can be used as an aid in determining therapeutic strategy. (12.5)**
- **Consider alternative treatment or treatment strategies in patients identified as CYP2C19 poor metabolizers. (2.3, 5.1)**

[16] In 2010, Paré et al. published a study that used genomic data collected in connection with two of Defendants' big trials. At trial, the companies'

Others appeared to validate the Mega study's findings.

One question the research raised was whether CYP2C19 loss-of-function alleles were related to one particular adverse outcome: blood clots blocking stents (stent thrombosis).

In a 2015 meta-meta-analysis, Osnabrugge et al. looked at 11 meta-analyses. They found a statistically significant relationship between CYP2C19 loss-of-function alleles and stent thrombosis.

But the Osnabrugge study also concluded that the 11 studies' results and conclusions were "discordant." It said the primary culprits of this disagreement were between study heterogeneity and publication bias. And it concluded "[c]onfidence in the presence of an association is limited, and personalized antiplatelet management based on genotyping is not

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witness, Dr. Roome, explained that Paré et al.'s article showed that "if you have genomic polymorphisms with loss of function on the CYP2C19, you do not have a worse outcome when you are treated by clopidogrel. You have an outcome that is comparable to those patients with no genomic polymorphisms on CYP2C19."

Dr. Gurbel, the State's witness, faulted Paré et al.'s study for excluding people with stents.

[17] In 2011, Holmes et al. published a meta-analysis that synthesized the results of 32 original research studies looking at whether CYP2C19 genotype could predict a person's response to clopidogrel. Holmes et al.'s meta-analysis found that there was "no evidence for a significant association between CYP2C19 genotype and any important cardiovascular outcome."

Dr. Gurbel criticized Holmes et al.'s work for relying on studies like CURE and CHARISMA, which had heterogeneous study populations. By casting such a wide net, he said, the meta-analysis "dilute[d] the signal of the importance of *2 [carriage]." Dr. Gurbel testified that if you just looked at people who'd had stents put in their hearts, then "the totality of the evidence [was] overwhelming" that there was a link between CYP2C19 genotype and clinical outcomes.

supported by the currently available evidence."

Osnabrugge's analysis suggested a possible correlation between CYP2C19 and stent thrombosis that was worth further exploration. Dr. Todd Seto, the medical director of the Center for Outcomes Research and Evaluation at Queen's Medical Center, testified that the "difficulties" in the 11 meta-analyses prevented Osnabrugge et al. drawing definite conclusions from the results.

Dr. Gurbel thought differently about Osnabrugge et al.'s findings. Concerning the link between CYP2C19 genotype and risk of stent thrombosis, he declared the "totality of the evidence . . . for stent thrombosis," was "irrefutable." "There's no argument against it. I mean, you have 11 meta-analyses reporting the same thing."

In September 2016, the FDA removed the statement that CYP2C19 poor metabolizers have worse clinical outcomes on Plavix from the boxed warning.[18]

[18] The 2016 Black Box label:

b. Suppressed research?

The second question the trial focused on was whether defendant companies suppressed research into Plavix's poor-responder issue to protect their profit margins. The State used internal documents and emails from the companies to support its allegation.

i. Internal Company Documents

First, the State pointed to the defendant companies' internal committee documents. They argued these established that the companies avoided research that could make Plavix look bad.

BMS and Sanofi have a jointly-staffed Plavix "Life Cycle Management" committee (LCM). The LCM is tasked with "discussing all the new data as well as major trials that were ongoing and sponsored by the companies" and "considering and approving or rejecting local studies from affiliates around the world."

WARNING: DIMINISHED ANTIPLATELET EFFECT IN PATIENTS WITH TWO LOSS-OF-FUNCTION ALLELES OF THE CYP2C19 GENE

See full prescribing information for complete boxed warning.

- **Effectiveness of Plavix depends on conversion to an active metabolite by the cytochrome P450 (CYP) system, principally CYP2C19. (5.1, 12.3)**
- **Tests are available to identify patients who are CYP2C19 poor metabolizers. (12.5)**
- **Consider use of another platelet P2Y12 inhibitor in patients identified as CYP2C19 poor metabolizers. (5.1)**

The minutes from LCM meetings in January 2001, June 2001, and June 2002 reveal that Defendants declined to fund local studies into variability of response to aspirin.

The minutes from 2001 reflect that the companies were concerned the studies into variability of response to aspirin might "lead to a similar trial on clopidogrel resistance." The June 2002 meeting minutes reflected that Defendants were continuing to refuse funding research into this area because it could lead to a "restrictive positioning of clopidogrel and could open the door to 'clopidogrel nonresponders.'"

Another document summarizing the LCM's activities in 2002 indicated that the committee rejected studies about aspirin nonresponsiveness because "it could lead to the same questions about clopidogrel and because the commercial sensitivity and science of studies in this field is being assessed at a corporate level first."

The June 2003 LCM meeting minutes noted the increase in publications concerning "[v]ariability of response with clopidogrel." They identified "[t]hreats for clopidogrel," related to variability, including "[p]otential threats for future sales."

Then the LCM outlined an "action plan" in 2003 concerning "clopidogrel response variability." The first item on the

action plan was a meta-analysis which would be done exclusively with already-collected data.

At trial, Dr. Dominique Roome, a Sanofi scientist who worked on Plavix-related issues from 1999 to 2011, conceded that their action plan did not include plans to conduct a large-scale clinical trial on the relationship between CYP2C19 genotype and clinical outcomes; but she explained this omission by saying that the issue of CYP2C19 poor metabolizers "wasn't even a question that was being discussed or debated in the scientific literature at that point."

ii. Internal Emails

The State also presented internal emails from the early and mid-2000s to demonstrate the companies' reluctance to engage in aspirin or clopidogrel-resistance studies.

In May 2000, a BMS researcher wrote his colleagues to propose a small, clinical trial "comparing the response of blacks vs. whites on ADP-induced platelet aggregation." A colleague recommended holding off on the study to see what questions the FDA would ask, noting that the "low number of black people" was not an issue for the FDA in the earlier CAPRIE study. He added that "[t]he problem is that, given the variability of the test, we always run the risk to show a difference in a pharmacology study . . . and then we really are in trouble." A counterpart at Sanofi agreed the proposed study

"could bear a significant risk" and suggested waiting to see if the FDA would bring it up.

In response to another proposed study on aspirin resistance in August 2002, a BMS scientist recounted that "Sanofi hs [sic] generally been 'down' on suggestions to study ASA [aspirin] resistance, because they are afraid that 'clopidogrel resistance' is right behind." He later wrote in a separate email:

> In my opinion, [Sanofi]'s/our reluctance to go down the path toward documentation of clopidogrel resistance is understandable, but it will catch up with us and perhaps be an unpleasant and costly surprise when others document it without asking our permission to do so.

In June 2003, BMS employees forwarded and discussed Dr. Gurbel's recently-published article on Plavix non-responsiveness. See supra Section II.B.2.a.ii.(1).

Three emails about Dr. Gurbel's article were presented at trial.

In the first, a BMS researcher wrote that he "view[ed] the paper with mixed feelings." He thought some of the data presented were "very positive and encouraging" but also noted that he had "received zero response internally" when he had asked for information on Plavix non-responders.

In the second email, the Vice President of U.S. Marketing for Plavix at the time shared the article and wrote that "BMS U.S. has had difficulty mobilizing the LCM to address the

importance of understanding Plavix resistance through our data and proactive research."

In the third email, the BMS Vice President for the "Sanofi Alliance" at the time wrote: "Sanofi had an in-house meeting on aspirin resistance in January and presented their data at the January LCM meeting. However, Sanofi remains adverse [sic] to doing any further work on either aspirin or clopidogrel resistance because of the potential negative marketing implications."

In 2005, the defendant companies determined at a meeting that "[a]dditional studies" were needed on the variability of platelet response issue and suggested using "small trials to help [Defendants] 'shape the debate.'"

In 2006, the defendant companies discussed variability of platelet response during an advisory board meeting. They concluded that while some researchers believed that variability corresponded with "clinical events," others disputed this relationship.

c. Consumer harm?

The last question was whether defendant companies' acts or practices harmed consumers. The evidence concerned contemporary understandings of (1) whether CYP2C19 genotype is linked to adverse clinical outcomes and (2) whether non-White

(particularly Asian) patients on Plavix are more likely to receive little or no benefit from the drug.

i. Clinical Outcomes

The State sought to support its theory that poor responders taking Plavix were at a higher risk of adverse clinical outcomes like heart attacks, strokes, or death. But this link is unclear.

In 2019, the State's witness, Dr. Gurbel, wrote that the link between poor responders and "major adverse cardiovascular events" on Plavix "remains controversial."[19] At trial, he emphasized that while the link between *major* adverse cardiovascular events is not clear, he was "100 percent certain" that a link between *adverse events* and poor response exists.

Dr. Laura Plunkett, the State's regulatory and pharmacology expert, agreed with Dr. Gurbel. She testified that "people that can't metabolize the drug, poor metabolizers, are at an increased risk of experiencing heart attacks and strokes." Dr. Plunkett elaborated on why poor responders are at an increased risk:

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[19] In an April 2010 editorial, Dr. Gurbel also wrote that:

> no single study has demonstrated a conclusive link between the presence of a loss-of function genetic polymorphism, suboptimal clopidogrel active metabolite generation (pharmacokinetic measurement), decreased clopidogrel responsiveness (pharmacodynamic measurement), and adverse clinical outcomes.

> if [poor responders] don't activate [Plavix], they can't get the benefit. And don't forget this is a drug that's being given to reduce the risk of life-threatening events -- heart attacks and strokes. So if you don't activate it and you're giving the drug to prevent that -- those events, then you're going to be at increased risk, because obviously without the drug there, you can't get the benefit.

Dr. Gurbel and Dr. Plunkett didn't think that poor responders were more likely to have adverse outcomes on Plavix because the drug was actively harming them. They thought, rather, that for those who didn't activate the drug *at all*, it was effectively a "placebo."

In response, the defendant companies focused on the difference between patients unable to metabolize the drug at all versus those who had a reduced but non-zero response to Plavix.

Dr. Seto testified that even a patient with two CYP2C19 loss-of-function alleles would still get some benefit from Plavix: "there are papers that have shown benefit in patients, including those who are poor metabolizers."

Dr. de Morais, the scientist who in 1994 identified the genetic mutation that causes poor responsiveness in CYP2C19, testified. She explained that CYP2C19 poor responders may still metabolize Plavix because "CYP2C19 is not the only enzyme. There are other enzymes that form the active metabolite." These other enzymes, she said "will pick up the tab [and metabolize]" Plavix if the CYP2C19 enzyme can't.

Adding to this, Dr. de Morais expounded on a "very unique" active metabolite that's produced when liver CYPs oxidize Plavix. Even for poor responders, patients can receive clinical benefits from Plavix, because the active metabolite forms a long-lasting, stable bond with blood platelets. This bond makes the platelets slippery so they cannot easily form a clot and stays slippery for a "couple of days or [a] week or so" before it's excreted from the body.

ii. Ethnicity and poor responsiveness

The State also attempted to show that Asian patients faced a greater risk of adverse effects on Plavix.

There was no dispute that Asians are more likely to carry the *2 or *3 CYP2C19 alleles than Whites. Dr. Gurbel elaborated that Asians have a 15% chance of carrying two loss-of-function alleles and a 50% chance of carrying one.

But the parties disagreed about whether Asian patients were likely to have worse outcomes on Plavix than White patients.

The defendant companies maintained that the drug worked for Asian patients. Dr. Seto testified that a 2005 study conducted at Queen's Medical Center found that ethnicity did not appear to affect the success rate or complication rate of procedures like stenting or angioplasty. Dr. Seto said the study confirmed that patients who were getting clopidogrel, "including Asians and our Pacific Islander patients," did fine.

For the State, Dr. Gurbel testified that Plavix was demonstrably less-effective for Asian patients. He compared the results of the CURE clinical trial (which had mostly White patients) with the COMMIT clinical trial (which had exclusively Chinese patients). He pointed out that Plavix had only a 9% risk reduction effect for the Chinese participants in the COMMIT trial, less than half of the 20% risk reduction shown in CURE. Thus, he reasoned, the COMMIT trial showed that Plavix was less effective for Chinese patients.

In response, Dr. Seto disagreed that the CURE and COMMIT studies – which used different methodologies – showed a reduced effectiveness in one group versus another. He testified that it was not possible to isolate if race or ethnicity was connected to any supposed difference in the results. He further noted that the 2016 American College of Cardiology/American Heart Association (ACC/AHA) guidelines recommend Plavix as an antiplatelet without any regard to patients' race or genetics. And that the guidelines recommend *against* routine genetic testing even for patients of Asian or Pacific Island descent.

3. FOF-COLs

In its Findings of Fact and Conclusions of Law, the court found that the companies had committed both deceptive and unfair acts. First, it stated that the companies had misled consumers by not informing patients about the poor responder issue from

the beginning. Second, the court determined that the companies engaged in a pattern and practice of suppressing inquiry into variability of response for financial reasons. Third, the court decided that the defendant companies' actions harmed Hawaiʻi consumers.

a. Deceptive Acts by Omission

First, the court focused on Plavix's labeling, stating that the "facts presented show that Defendants had sufficient knowledge, technology, and ability to update the Plavix label from launch and continuing for many years."

The court listed various facts that Defendants knew at the time of Plavix's launch. It highlighted these findings: (1) Defendants' internal reports revealing that the Cytochrome P450 enzymes, including CYP2C19, were involved in Plavix's metabolization; (2) Defendants' 1998 meta-analysis finding that 32.2% of patients had a reduced response to Plavix when one test was used;[20] (3) the CAPRIE clinical trial's showing of a statistically significant difference in Plavix's effectiveness for White patients as compared to non-White patients; (4) Dr. de Morais' work showing that "CYP2C19 polymorphisms were found to be a 100% predictor of poor metabolizers (for S-

[20] In a footnote, the trial court "consider[ed] it significant that Defendants did not disclose their 1998 Meta-Analysis to the FDA until after [the] Gurbel study was published." See supra Section II.B.2.a.ii(1).

mephenytoin[21])"; (5) East Asians were "five-fold" more likely to have a variant of CYP2C19 that made them Plavix poor responders; and (6) a genetic test for CYP2C19 variations had existed for laboratory use since 1994.

The court found that after Dr. Hulot's 2006 study supporting the hypothesis that CYP2C19 polymorphisms contribute to Plavix variability of response "Defendants took no action to update Plavix's label to inform prescribing physicians and patients about Plavix resistance" even though "it was already established that these CYP2C19 polymorphisms were more prevalent among certain Asian populations."

The court concluded the companies failed to use the information they had about Plavix's variability of response to "try to warn the public or the FDA" about the poor responder issue or pursue information about Plavix's bioactivation.

b. Suppressed and Avoided Research

Second, the court faulted Defendants for avoiding any serious examination into CYPC219's role in driving variability of response to Plavix. It rejected Defendants' claim that they had supported clinical trials looking into variability of response.[22]

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[21] Unlike Plavix, S-mephenytoin is a drug almost exclusively metabolized by CYP2C19.

[22] In rejecting this argument, the court relied on Dr. Gurbel's testimony that Defendants "didn't . . . I would say broadly, you know, [do] any

The court found the companies "evidenced a clear intent not to conduct or sponsor any research that might confirm the existence of and/or reason for 'Plavix resistance' or 'Variability of Response' to a patient's race or other identifiable genetic factors."

It further noted that the companies had a duty to investigate why some patients had a diminished response to Plavix. The court cited Dr. Plunkett's testimony that pharmaceutical companies must continue to investigate potential issues with the drugs they sell: "under Section 21 CFR [§] 314, there are specific requirements for companies to perform this type of surveillance of their drugs and the literature . . . in order to understand whether or not there are risks out there"[23] and that this affirmative behavior is "part of good pharmacovigilance practice."

The court also rejected Defendants' claim that they "did not investigate the impact of CYP2C19 polymorphisms on Plavix

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meaningful research, no." The court also cited Dr. Plunkett's testimony that "I haven't seen a large clinical trial that has been done by the company or anyone else of the power to be able to answer definitively those questions, and specifically for the individuals that carry two loss-of-function alleles, we haven't completely defined that. No study has been done."

[23] More specifically, 21 CFR §§ 314.80 (Postmarketing reporting of adverse drug experiences) and 314.81 (Other postmarketing reports) impose a broad duty of surveillance. 21 CFR §§ 314.80(b) requires, for example, "prompt[] review [of] all adverse drug experience information obtained or otherwise received by the applicant from any source, foreign or domestic, including information derived from commercial marketing experience, postmarketing clinical investigations, postmarketing epidemiological/surveillance studies, reports in the scientific literature, and unpublished scientific papers."

Variability of Response because they believed at the time of launch and for many years afterward" that CYP3A4 was the "primary means by which a patient's body produced Plavix's active metabolite." The court said it found "much more persuasive the words and actions reflected in Defendants' corporate records, and testimony consistent with them, which evidence a clear intent by Defendants to avoid any studies that might unearth negative information about Plavix."

The court said Defendants' records showed that their aversion to certain variability of response research was "tied to concerns about the potential impact of adverse clinical trial results on sales of the drug."

The court made a series of factual findings concerning Defendants' internal records. For example, it referenced emails from 2000 where Defendants shot down a proposed study comparing clopidogrel response in Black versus White patients as risky. It then quoted a 2001 document showing that the LCM had rejected a proposed study on aspirin resistance because "it could lead to a similar trial on [Plavix] resistance." The court also cited two 2002 LCM documents reflecting the committee's decision to reject aspirin studies "because they 'could lead to the same questions about [Plavix],' they 'could open the door to "[Plavix] non-responders,"' and because there was 'no commercial interest' in such studies."

The court also emphasized how the companies' behavior undermined their claim that they believed CYP3A4 primarily metabolized Plavix. It pointed to a November 2005 meeting summary (after the COMMIT study was published) where Defendants observed that they could support "small trials" on the variability of platelet response issue that could help them "shape the debate."

c. Consumer Harm

Lastly, the court found that the companies' behavior harmed consumers.

The court relied on the label's materiality to reach its conclusion. It noted that boxed warnings are usually reserved "for serious warnings, particularly those that may lead to death or serious injury." In response to Defendants' argument at trial that "the 2016 boxed warning deleted any reference to a causal relationship between CYP2C19 poor metabolizer status and clinical outcomes," the court said that "since the boxed warning remains on the Plavix label, Defendants' argument is unpersuasive."

The court found that poor responders to the drug "receive only partial benefit or risk reduction, which may be insufficient to prevent an adverse event." It cited to studies from the later 2000s showing "CYP2C19-based poor responsiveness to Plavix led to an increased risk of cardiac events . . . when

compared to patients who were normal or intermediate responders." It also found that "the evidence presented at trial established that Defendants knew . . . at the time of [Plavix's] launch . . . that Plavix patients who are poor metabolizers are likely at higher risk of a recurrent heart attack or stroke than those who are not poor metabolizers."

The court's finding about the increased risk for cardiovascular events faced by CYP2C19 poor metabolizers underpinned its conclusions that Defendants' omission was likely to mislead consumers. This finding also partly supported the court's unfair acts or practices ruling, in particular, that the defendant companies' "conduct was substantially injurious to consumers." That finding, in turn, informed the court's analysis of the "injury to the public" prong of its penalty calculation.

The court did not explicitly find that Asian patients were exposed to a high risk of adverse cardiac outcomes while taking Plavix. But it referenced the notion that Plavix doesn't work as well for non-Whites in its analysis of the injuries inflicted on consumers. For example, the court highlighted Dr. Gurbel's testimony comparing the COMMIT and CURE clinical trials. It detected "a statistically significant disparity in the number of adverse events suffered by non-[W]hite racial groups."

The court then linked Defendants' awareness (from the

CAPRIE clinical trial) that Plavix was less effective for non-Whites to their "intent not to conduct or sponsor any research that might confirm the existence of and/or reason for 'Plavix resistance' or 'Variability of Response' to a patient's race or other identifiable genetic factors."

From this, the court concluded that the companies "took no action to update Plavix's label to inform prescribing physicians and patients about Plavix resistance" in spite of the "established" fact that "CYP2C19 polymorphisms [leading to poor response] were more prevalent among certain Asian populations."

4. Appeal

Defendants appealed the circuit court's judgment to the Intermediate Court of Appeals. We granted the State's petition for transfer to this court.

On appeal, Defendants challenge nearly all the circuit court's findings of fact and conclusions of law.

Defendants contend the evidence showed they didn't know about the CYP2C19 metabolization issue until the Mega study came out in December 2008. So, they argue, there is nothing "deceptive" or "unfair" about their failure to update the Plavix label with poor responder information before then.

Defendants stress that they investigated Plavix's safety and efficacy throughout the 2000s, and they claim that they decided against funding certain studies into variability of

response because of those studies' size and design limitations, not because they were trying to protect their profits.

Defendants also emphasize the lack of evidence showing the omission of the poor responder information from Plavix's label injured anyone. Even poor responders, Defendants assert, can benefit from Plavix.

In addition to challenging the substance of the court's holding, Defendants also raise procedural defenses.

First, they argue that the State's claims about Plavix's FDA-approved label are barred by UDAP's "safe harbor" provision, which exempts from UDAP "[c]onduct in compliance with the orders or rules of, or a statute administered by, a federal, state, or local governmental agency." HRS § 481A-5(a)(1) (2008). Defendants say that because the FDA approved Plavix's label they are "in compliance" with the FDA's regulations and exempt from liability under UDAP.

Second, the companies claim that the State's suit is time-barred by UDAP's four-year statute of limitation.

Third, they claim the State's UDAP claims are preempted by the Federal Food, Drug, and Cosmetic Act (FDCA) because it would be "impossible" for the companies to comply with both the federal law on drug labeling and the duties imposed by Hawaiʻi law.

III. DISCUSSION

A. No Procedural Bars to the State's Claims

First, we address the defendant companies' procedural arguments. Neither the UDAP's safe harbor provision nor its statute of limitations bar the State's claims. The claims are also not preempted by federal law.

1. No Safe harbor

The UDAP's safe harbor provision does not block the State's action.

UDAP's "safe harbor" exempts "[c]onduct in compliance with the orders or rules of, or a statute administered by, a federal, state, or local governmental agency." HRS § 481A-5(a)(1).

Courts interpreting safe harbor provisions often do so narrowly, holding they bar only conduct which is not specifically allowed or required by another authority. See Showpiece Homes Corp. v. Assurance Co. of Am., 38 P.3d 47, 56 (Colo. 2001) (explaining that "[c]onduct amounting to deceptive or unfair trade practices . . . would not appear to be 'in compliance' with other laws" where it was not specifically authorized by those laws).

The FDA did not issue the companies a special dispensation absolving them of any state-law duties they may have (above and beyond their obligations under federal law) to update the Plavix label as the relevant science evolves. The FDA's approval of

Plavix's label does not confer the agency's imprimatur on the companies' decision not to add information about variability of response to its warnings before 2009. And Defendants have not pointed to any federal statutes specifically authorizing the omissions and conduct the State alleges violates the UDAP.

This is not an old-fashioned false advertising consumer protection case. The State's allegations and the circuit court's FOFs and COLs are concerned with Defendants' conduct, not only the contents of the Plavix label. The State's UDAP allegations also expressly involve Defendants' approach to publicizing and investigating the variability of response issue. Defendants offer no explanation of why UDAP's safe harbor should bar the claims that, for instance, Defendants violated the law by failing to disclose the results of their 1998 meta-analysis to the public or by avoiding research on variability of response to protect their profits.

Because there is no federal or state law, order, or rule expressly authorizing the omissions the State claims violated the UDAP, and because of the conduct-centric nature of the State's allegations, we hold that the UDAP's safe harbor provision does not bar the State's claims.

2. No Statute of Limitations

The State's action is not time-barred.

Under HRS § 657-1.5 (1993), the State is not subject to any

limitations periods unless it is "specifically designated in such a statute as subject to the limitation period contained therein."

Defendants maintain that HRS § 480-24(b) (2008) "specifically designated" the State as subject to HRS § 480-24(a)'s four-year limitations period. But it does not.

A statute does not "specifically designate" the State as subject to its statute of limitations unless it clearly and unambiguously provides that its limitations period applies to the State. HRS § 480-24(b) identifies three situations in which the State is exempted from subsection (a)'s statute of limitations.[24] But while those exemptions may *imply* that the

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[24] HRS § 480-24(b) (2008) provides:

> (b) The following shall toll the time for commencement of actions by the State under this chapter if at any time:
>
> (1) Any cause of action arising under this chapter accrues against any person, the person is out of the State, the action may be commenced within the terms respectively limited, after the return of the person into the State, and if, after the cause of action has accrued, the person departs from and resides out of the State, the time of the person's absence shall not be deemed or taken as any part of the time limited for the commencement of the action.
>
> (2) Any cause of action arising under this chapter accrues against any person, the person has petitioned for relief under the bankruptcy code, the time during which the bankruptcy case is pending shall not be deemed or taken as any part of the time limited for the commencement of the action.
>
> (3) Any cause of action arising under this chapter accrues against any person, there is a criminal action pending which arises out of the same occurrence, the time during which the criminal action is pending shall not be deemed or taken as any part of the time limited

State is subject to HRS § 480-24(a)'s limitations period, they do not unambiguously and expressly state that HRS § 480-24(a)'s limitations period applies to the State.

Under HRS § 657-1.5, then, the State is not subject to the limitations period contained in HRS § 480-24(a).[25]

3. No Preemption

Federal law does not preempt the State's claims.

The companies assert this case is one of implied conflict preemption, that is, Hawai'i law conflicts with or contradicts federal law. See Rodrigues v. United Pub. Workers, AFSCME Local 646, AFL-CIO, 135 Hawai'i 316, 323, 349 P.3d 1171, 1178 (2015) (defining "implied conflict preemption" as "when state law is in actual conflict with federal law.") (citation omitted). If "it is impossible for a private party to comply with both state and federal requirements," then implied conflict preemption occurs.

> for the commencement of the action. As used in this paragraph, a criminal action is pending until its final adjudication in the trial court.

[25] The legislative history to the 2016 amendment repealing HRS § 480-24(b) supports this conclusion. The House bill that eventually became that amendment observed:

> In the context of claims brought by the State and its agencies pursuant to chapter 480 of the Hawai'i Revised Statutes, the Hawai'i legislature has never specifically designated the State or its agencies as being subject to any limitation period. Consequently, no limitation period can apply to actions brought by the State under chapter 480, Hawai'i Revised Statutes.

House Bill No. 2329, A Bill for an Act Relating to Consumer Protection. https://www.capitol.hawaii.gov/session2016/bills/HB2329_.pdf [https://perma.cc/C3FT-AHDF].

Hawaii Mgmt. All. Ass'n v. Ins. Comm'r, 106 Hawai'i 21, 30, 100 P.3d 952, 961 (2004) (cleaned up)).

The companies argue there was no way they could have updated Plavix's label to provide the warning the State says UDAP requires and at the same time comply with federal law.

The Defendants overstate the differences between state and federal law. The fact that state law imposes a greater duty to warn on drug makers than the FDA, does not give rise to implied conflict preemption.[26] On the other hand, if a drug maker cannot comply with both the labeling duties imposed by the FDA and its duties under state law, "federal law controls and . . . state-law tort claims must be dismissed." Guilbeau v. Pfizer Inc., 880 F.3d 304, 310 (7th Cir. 2018).

Generally, drug manufacturers only update their products' labels once the FDA has approved a supplemental application. But under the agency's CBE regulation:

> if a manufacturer is changing a label to "add or strengthen a contraindication, warning, precaution, or adverse reaction" or to "add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the drug product," it may make the labeling

[26] See Motus v. Pfizer Inc., 127 F. Supp. 2d 1085, 1092 (C.D. Cal. 2000) ("[M]ost courts have found that FDA regulations as to design and warning standards are minimum standards which do not preempt state law . . . failure to warn claims."); Wells v. Ortho Pharm. Corp., 788 F.2d 741, 746 (11th Cir. 1986) ("An FDA determination that a warning is not necessary may be sufficient for federal regulatory purposes but still not be sufficient for state tort law purposes."); Hill v. Searle Lab'ys, a Div. of Searle Parms., Inc., 884 F.2d 1064, 1068 (8th Cir. 1989) ("FDA approval is not a shield to liability. . . . FDA regulations are generally minimal standards of conduct unless Congress intended to preempt common law, which Congress has not done in this area.").

> change upon filing its supplemental application with the FDA; it need not wait for FDA approval.

Wyeth v. Levine, 555 U.S. 555, 568 (2009) (quoting 21 CFR §§ 314.70(c)(6)(iii)(A), (C)).

In Wyeth, the Supreme Court said that the maker of a prescription drug could establish that it was impossible for it to comply with both state law and the FDCA with "clear evidence that the FDA would not have approved a change to [the brand name drug's] label" required by state law. Id. at 571. "Clear evidence" that the FDA would not have approved a change requires a showing that the drug maker "fully informed the FDA of the justifications for the warning required by state law and that the FDA, in turn, informed the drug manufacturer that the FDA would not approve changing the drug's label to include that warning."[27] Merck Sharp & Dohme Corp. v. Albrecht, 139 S. Ct. 1668, 1678 (2019).

Here, Defendants have not provided "clear evidence" that the FDA *would have* rejected an earlier label-update proposal. In fact, as the State points out, the record shows that the FDA eventually put information about the poor responder issue in a

[27] The drug maker need not show that the FDA formally rejected the proposed label change, just that it *would have* rejected it had it been sought. See In re Zofran (Ondansetron) Prod. Liab. Litig., 541 F. Supp. 3d 164, 203 (D. Mass. 2021) ("Multiple courts have found [conflict] preemption where the manufacturer had not requested the precise warning sought by the plaintiffs when the FDA had nonetheless made it clear that it would not accept that label change."); Seufert v. Merck Sharp & Dohme Corp., 187 F. Supp. 3d 1163, 1170 (S.D. Cal. 2016) ("[M]anufacturer submission of a proposed labeling change is relevant, but not dispositive, in determining whether a defendant can establish conflict preemption.").

black box warning on Plavix's label. It's conceivable that the FDA would have rejected any pre-Mega study attempts to update Plavix's label on the grounds that the CYP2C19 poor responder information wasn't necessarily clinically relevant. But there's no "clear evidence" that would have happened.

Defendants' contention that they could not have used the CBE regulation to update Plavix's label before December 2008 because CBE-updates are only allowed when drug makers have "new information" about a drug is unconvincing. Wyeth considered - and rejected - the drug maker's similar argument that it could not have used the CBE regulation to update its label with a warning required by state law because it did not have "newly acquired information" about its product.[28] The FDA's definition of "'newly acquired information' is not limited to new data, but also encompasses 'new analyses of previously submitted data.'" Wyeth, 555 U.S. at 569 (citation omitted).

The FDA's expansive definition of "newly acquired information"[29] drowns Defendants' preemption claim. If, as the

[28] The Court explained that this broad definition of newly acquired information "accounts for the fact that risk information accumulates over time and that the same data may take on a different meaning in light of subsequent developments." Wyeth, 555 U.S. at 569.

[29] The definition of "newly acquired information" provided in 21 CFR § 314.3(b) is:

> Newly acquired information is data, analyses, or other information not previously submitted to the Agency, which may include (but is not limited to) data derived from new clinical studies, reports of adverse events, or new

State alleges, Defendants knew enough about the poor responder issue to trigger a duty under state law to update the Plavix label, then they would also have enough "newly acquired information" to effectuate that update through the CBE regulations.

Defendants have not established it would have been impossible under federal law for them to add information about the poor responder issue to the Plavix label.

B. Summary judgment on materiality

We now turn to the circuit court's summary judgment ruling on materiality.

The defendant companies argue that the court erred by granting partial summary judgment to the State on materiality. They also argue the court made an "alternative" ruling that ignored the summary judgment framework. We agree.

We review a trial court's grant of summary judgment de novo. Umberger v. Dep't of Land & Nat. Res., 140 Hawai'i 500, 512, 403 P.3d 277, 289 (2017). Because materiality is "ordinarily for the trier of fact," summary judgment on this element is "often inappropriate." Courbat, 111 Hawai'i at 263, 141 P.3d at 436 (cleaned up).

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analyses of previously submitted data (e.g., meta-analyses) if the studies, events, or analyses reveal risks of a different type or greater severity or frequency than previously included in submissions to FDA.

Here, the summary judgment grant was inappropriate for two reasons. First, the circuit court disregarded evidence that raised genuine factual disputes about the materiality of the information in the 2010 Black Box Warning. Second, calling itself the "Ultimate Trier of Fact," the court made an alternative ruling and weighed evidence before trial, finding materiality, and straying from the summary judgment framework.

We vacate both the court's "traditional" and "alternative" summary judgment rulings.

1. Disregarded Evidence

Under UDAP, a representation or omission is considered material if it "involves information that is important to consumers and, hence, likely to affect their choice of, or conduct regarding, a product" — in this case, Plavix. Courbat, 111 Hawaiʻi at 262, 141 P.3d at 435 (cleaned up). The test is objective, not subjective. Id. It considers the viewpoint of the "reasonable consumer, not the particular consumer." See Yokoyama v. Midland Nat'l Life Ins. Co., 594 F.3d 1087, 1092 (9th Cir. 2010).

Urging summary judgment, the State argued that the information placed in the 2010 boxed warning was material to consumers. The State stressed that a black box warning is the most serious warning the FDA can require. Both BMS and the FDA considered the information on this label "the most important

information." It also presented eight survey findings from the defendant companies' 40-doctor telephone survey on how the boxed warning impacted the doctors' prescribing behavior.

The defendant companies did not deny that black box warnings are important in the abstract. Rather, they argued that in this case, no speculation was necessary about whether the label information relating to poor-responders was "likely" to affect doctors' prescribing decisions. There was already a decade of evidence about what Hawaiʻi doctors actually did in response to the label change: not much.

Their expert testimony, the companies said, "uniformly demonstrates that the boxed warning did not affect [doctors'] prescriptions of Plavix." The companies stressed that the Hawaiʻi doctors said that their clinical practices were not impacted by the disclosure of information about CYP2C19 poor metabolizers.

Dr. Todd Seto, for example, stated that even though 70 percent of his patients are of Asian or Pacific Island descent, the black box warning hasn't affected his practice. He maintained that "nearly all" the angioplasty patients at Queen's Medical Center in Honolulu take Plavix. Dr. Seto also said that he was "not aware" of any physician at Queen's who "conducts routine genetic testing before prescribing Plavix" to determine if someone is a poor responder.

The companies also pointed to evidence from the State's public health journal: it recommended that Hawaiʻi doctors not change their prescribing practice based on the boxed warning and that genetic testing not be done. Adding to that, State public health agencies reimburse for Plavix without regard to race or genotype and without requiring genetic testing. Further, the companies said, Hawaiʻi Medicaid reimbursements of Plavix increased after the boxed warning, including for patients of most Asian ethnicities.

Taken in the light most favorable to them, the companies argued, the black box warning did not change the medical community's prescribing practices or genetic testing practices. They maintained that consumers continued to take Plavix despite the warning, raising a strong inference that the warning was not material to consumers.

The circuit court disagreed. It rejected the companies' materiality evidence, finding that when information relates to safety and health, there's a presumption that it's material. Since materiality is determined by an objective, patient-oriented test, evidence about the behavior of doctors could never create a genuine issue of material fact. The court ruled that the defendant companies failed to overcome the materiality presumption.

The court erred. First, it overstated the presumption of materiality. Second, in refusing to consider any evidence about doctors' prescribing behavior, the court misinterpreted the objective, patient-centered materiality test.

The presumption of materiality that the court relied on comes from the deceptive advertising context. See Novartis Corp. v. F.T.C., 223 F.3d 783 (D.C. Cir. 2000); In re Thompson Med. Co., Inc., 104 F.T.C. 648 (1984); In re Simeon Mgmt. Corp., 87 F.T.C. 1184 (1976).[30]

A presumption of materiality does not end things. It's not "an inflexible rule that eliminates [the] need to look at materiality on a case-by-case basis." Thompson Med., 104 F.T.C. at 648 n.45. Overcoming the presumption of materiality is "not a high hurdle." In re Novartis Corp., 127 F.T.C. 580, 686 (1999). Defendants may always counter the presumption with extrinsic evidence, including "expert testimony, consumer research, and evidence of how the networks and other expert bodies interpreted the advertisements." Thompson Med., 104 F.T.C. at 24.

The State's materiality argument is ultimately one from intuition – the intuition that something the FDA considers *very*

[30] The State only cited Novartis Corp. v. F.T.C. for its presumption of materiality argument. And the court cited only one case that concerned an *omission*, rather than affirmative deception. It involved a company that advertised its product as medical but did not tell consumers the product was not FDA-approved. In re Simeon Mgmt., 87 F.T.C. 1184. This case did not mention a presumption of materiality.

important for consumers to see must be material to those consumers.

But materiality is about what consumers do, not what the FDA thinks. See In re ConAgra Foods, Inc., 90 F. Supp. 3d 919, 1020 (C.D. Cal. 2015) (in misleading marketing case the "relevant question" was not whether the FDA requires that GMO food be labeled non-natural, but rather, how a "reasonable consumer" would have understood the term "100% Natural" and whether it would have been "material to [their] purchasing decision"). If the companies are able to present evidence that the information did not, in fact, change consumer behavior, they are entitled to do so.

Nor are the companies' statements that they considered the label information "important" a slam-dunk for the State. Because the standard is whether the information is material to a *reasonable consumer*, not the defendants. See Courbat, 111 Hawaiʻi at 262, 141 P.3d at 435; see also In re McCormick & Co., Inc., Pepper Products Mktg. & Sales Practices Litig., 422 F. Supp. 3d 194, 250 (D.D.C. 2019) (observing that "evidence of a defendant's opinion as to materiality is not an adequate substitute for extrinsic evidence.").

In short, the circle of what the FDA and the companies consider "important" may not wholly overlap with the circle of what consumers consider "material" to their decisions.

The same can be said for what *doctors* consider important. But while the prescribing decisions of doctors are not synonymous with consumer behavior, they are certainly not irrelevant to it.

The reality is that patients do not operate in a vacuum when making decisions about prescription drugs. Objectively reasonable patients may rely on their doctors to help them make sense of drug labels. See In re Reglan Litig., 142 A.3d 725, 738 n.8 (N.J. 2016) ("While the drug labels are initially disseminated to doctors and pharmacists, they, in turn, inform their patients, passing the warnings on to consumers.").

So, while patients and doctors cannot be conflated, the testimony of prescribing doctors also cannot be completely written off. The fact that cardiologists in Hawaiʻi continued to prescribe Plavix to patients of all ethnicities even after the introduction of the black box warning bore on whether a "reasonable" patient would choose to purchase the drug. The circuit court erred by shutting out this category of evidence entirely.

The substantial evidence and testimony the defendant companies mustered that Hawaiʻi doctors did not change their Plavix prescribing practices after the placement of the label and did not recommend genetic testing to patients was enough to

create a genuine dispute of material fact on materiality. To hold otherwise was error.

2. Alternative Ruling

The circuit court gave a back-up explanation for granting the State's partial summary judgment motion. This alternative ruling involved the court weighing the evidence as if it were trying the case. The court felt "confident" it "would reach the same conclusion" if the materiality issue were presented at trial. So it ruled on materiality at the summary judgment stage, disregarding the summary judgment framework: "When ruling on summary judgment prior to a bench trial — as here — the court need not resolve inferences in favor of the non-moving party."

That is not how summary judgment works. A court must consider the evidence "in the light most favorable to the non-moving party" at summary judgment. Ralston v. Yim, 129 Hawaiʻi 46, 56, 292 P.3d 1276, 1286 (2013) (cleaned up). The moving party bears the burden of persuasion. Yoneda v. Tom, 110 Hawaiʻi 367, 384, 133 P.3d 796, 813 (2006). To prevail, the moving party must demonstrate that there's no genuine dispute about the material facts and the "undisputed facts" show the court should grant summary judgment as a matter of law. Id. (citing Lee v. Puamana Cmty. Ass'n, 109 Hawaiʻi 561, 567, 128 P.3d 874, 880 (2006)).

Whether a motion for summary judgment is brought in a jury trial or a bench trial makes no difference. A judge deciding a summary judgment motion may not fact-find, even if the matter is set for a for a bench trial. See Anderson v. Liberty Lobby, Inc., 477 U.S. 242, 249 (1986) ("[A]t the summary judgment stage the judge's function is not himself to weigh the evidence and determine the truth of the matter but to determine whether there is a genuine issue for trial.")

Summary judgment is no substitute for trial. The record is thinner. There's no cross-examination. The court has seen only a small snapshot of the case. An improvident grant of summary judgment denies a party the chance to fully mount an offense or defense.

That is why the summary judgment process has a safeguard – the inference in favor of the non-moving party. Ralston, 129 Hawaiʻi at 56, 292 P.3d at 1286; see also Nolan v. Heald College, 551 F.3d 1148, 1154 (9th Cir. 2009) (trial court that weighed evidence at the summary judgment stage "ignor[ed] the protections that summary judgment usually affords the non-moving party"). Without this safeguard, summary judgment would end-run the trial right.

The circuit court deviated from the normal summary judgment framework. The court found a material fact – materiality - before trial, supporting its "alternative ruling" with a

citation to TransWorld Airlines, Inc. v. Am. Coupon Exch., Inc., 913 F.2d 676 (9th Cir. 1990), recommended by the State. Quoting the Ninth Circuit, the court said: "where the ultimate fact in dispute is destined for decision by the court rather than by a jury, there is no reason why the court and the parties should go through the motions of a trial if the court will eventually end up deciding on the same record." TransWorld, 913 F.2d at 684.

TransWorld did not prod trial judges to weigh facts at the summary judgment stage. Rather, in TransWorld the court scolded the judge below for skipping to summary judgment on a "wholly inadequate" factual record. Id. at 683 ("[W]e conclude that the record is wholly inadequate, and the district court's own opinion is the most persuasive testimony to that inadequacy.").

TransWorld acknowledged that when a question was pure law, where trial would not alter the factual record, there is no need to "go through the motions of trial." Id. at 684. But, the court stressed, "courts must not rush to dispose summarily of cases — especially novel, complex, or otherwise difficult cases of public importance — unless it is clear that more complete factual development could not possibly alter the outcome and that the credibility of the witnesses' statements or testimony is not at issue." Id. at 684-85.

For a case like this one – novel, complex, and of great public importance – a developed factual record is essential to a fair trial.

Here, the court found the defendant companies' evidence "weak and unpersuasive." It said that "even" if the Defendants presented other evidence, "this Court is convinced that if the issue of materiality were litigated at trial the Court would ultimately conclude that the information in the Black Box Warning is material."

Trial courts have no business factfinding at the summary judgment stage. We vacate the court's alternative ruling.

C. UDAP – Deceptive Acts or Practices

The court's grant of summary judgment on materiality reverberated throughout the trial. Because the materiality ruling formed the basis of the court's holding that the defendant companies committed deceptive acts or practices, we vacate this part of the holding.

Materiality is an essential element of a UDAP deceptive acts violation. See Courbat, 111 Hawaiʻi at 262, 141 P.3d at 435 (To prove a deceptive act or practice under UDAP, a plaintiff must show "(1) a representation, omission, or practice that (2) is likely to mislead consumers acting reasonably under the circumstances where (3) the representation, omission, or practice is material.") When the court issued its findings of

fact and conclusions of law, it remarked that it had "already determined that the information in the 2016 boxed warning was material." But we have vacated that determination. Materiality is now an unproven element. The deceptive acts holding based on it cannot stand.

For deceptive acts liability, the court must also find that the omission in question was likely to mislead consumers. In its decision, the court found that "the omission of this *material* information was likely to mislead consumers." (Emphasis added.) This phrasing suggests that the court found the omission likely to mislead consumers in part or in whole because it was an omission of *material* information. This throws the other main element of deceptive acts liability into doubt as well.

Lack of an essential element (or two) is enough to vacate a result. But the materiality ruling marred the trial outcomes in other, more far-reaching ways. In its summary judgment order, the court ruled that evidence of "what's happening in Hawaiʻi," such as "prescription practices and genetics testing practices" after the 2010 Black Box Warning could not be introduced at trial. The court drew a thick line in the sand: it would not hear medical expert testimony on anything that happened after 2010, when the FDA first placed its boxed warning on Plavix.

Based on its materiality ruling, the court granted a motion in limine by the State to substantially limit the testimony of Defendants' main expert witnesses, three Hawaiʻi cardiologists. These doctors were not allowed to testify about "their own practices regarding use of Plavix" after 2010. Nor could they provide any opinions based on "medical or scientific literature" that drew upon post-2010 data.

Defendants had wanted to argue that the Plavix story didn't end in 2010. Hawaiʻi doctors continued to treat patients of all ethnic backgrounds with Plavix, guidelines continued to recommend Plavix treatment, and in 2016, the FDA walked back part of its 2010 warning, removing language that warned of worse clinical outcomes for CYP2C19 poor-responders. But Defendants could not make this argument; their expert witnesses were not allowed to discuss any of it.

At the heart of the State's case is the notion that, for a large chunk of Hawaiʻi's population, Plavix is a bad drug, little better than a placebo. Bristol-Myers Squibb and Sanofi vehemently disagree. But unlike the State, they did not have the chance to make their case fully at trial. We therefore vacate the circuit court's deceptive acts holding.

D. UDAP – Unfair Acts or Practices

Unfair act UDAP claims are distinct from deceptive act UDAP claims. To violate HRS § 480-2, a plaintiff may show that an

act or practice is deceptive *or* unfair. See Bronster v. U.S. Steel Corp., 82 Hawaiʻi 32, 50-51, 919 P.2d 294, 312-13 (1996) (jury instructions wrongly conflated deceptive acts and unfair acts under UDAP). A practice is unfair if it (1) offended public policy, (2) was immoral, unethical, oppressive, or unscrupulous, or (3) substantially injured Hawaiʻi consumers. See Hungate v. Law Office of David B. Rosen, 139 Hawaiʻi 394, 411, 391 P.3d 1, 18 (2017).

The circuit court found that the defendant companies violated the UDAP in each unfair acts or practices way.

We conclude that the court's materiality ruling affected its unfair acts finding on "substantial injury." The State, however, proved separate and independent grounds to find the defendant companies' conduct offended public policy and was immoral under UDAP. These findings support the court's unfair acts holding.

1. No Substantial Injury

The Defendants argue that the court's unfair acts holding must meet the same fate as its deceptive acts holding. Because both were impermissibly tainted by the materiality ruling, neither can stand.

The companies acknowledge, as they must, that materiality is not an element of unfair act claims. But they maintain that the court's premature materiality ruling prevented them from

mounting a complete defense on their unfair acts or practice claim. And they point to language in the court's holding that assumed the materiality of the black box warning.

We agree – up to a point.

The circuit court found the companies' conduct unfair by every possible measure: it was against public policy; it was immoral, unethical, and unscrupulous; *and* it was substantially injurious to consumers.

The court's misplaced materiality ruling played a part in some of these findings. Most significantly, it impacted the court's finding that the companies' conduct substantially injured consumers.

Substantial injury, more so than the other unfair prongs, focuses on consequences for consumers. Defendants' most basic argument against materiality – that in practice, the information in the black box did not matter and patients were not harmed by its absence – goes to substantial injury just as much as it goes to materiality. And the evidence that Defendants wished to but could not introduce about what actually happened after 2010 is probative to the question of consumer injury.

The court first found that consumers were injured because they were denied "the opportunity to consider whether to undergo genetic testing" to determine their response to Plavix. At summary judgment, Defendants mustered evidence that Hawaiʻi

hospitals and doctors do not currently perform genetic testing before prescribing Plavix. If patients aren't given genetic testing before taking Plavix *now*, Defendants argued, how were they harmed by not having genetic testing *then*? This evidence and this argument were not tested at trial. The court prevented the companies from introducing any evidence of medical practices after 2010, including genetic testing practices.

Second, the court found that "patients with CYP2C19 loss-of-function alleles" were injured because they were deprived of "the opportunity to make informed decisions" about taking Plavix versus an alternative treatment. For a lack of information to harm consumers, that information must be material to them. It may well have been. But because the court prematurely decided the materiality issue, findings of harm to consumers that hinge on that materiality also cannot stand.

The court similarly found that patients were harmed because they could not "give informed consent to their treatment." This more broadly-phrased restatement of the court's second finding fails for the same reason.

Lastly, the court found that the defendant companies harmed "an indeterminate number" of patients who were deprived of the "intended risk reduction [they] were relying on Plavix to provide." This holding also rests on a chain of assumptions that the materiality ruling prevented the Defendants from

contesting. Namely, Defendants were foreclosed from arguing that if doctors do not currently test patients for CYP2C19 alleles before prescribing and still prescribe Plavix regularly across ethnic groups, it is reasonable to infer that the medical community thinks Plavix provides adequate risk reduction. Doctor testimony on their current practice is plainly relevant to the question of whether a drug substantially injures patients by providing lower risk reduction, but the court's materiality ruling effectively barred that testimony.

Materiality mattered for each of the court's substantial injury findings. So we throw out that portion of the court's unfair act holding.

2. Hawaiʻi Unfair Acts or Practices Law

Substantial injury is out. Under the Federal Trade Commission Act – the original inspiration for UDAP - this would be the end of the matter: no substantial injury, no unfair acts claim.

But under Hawaiʻi law, the State didn't need to run the table on unfair conduct. Our UDAP caselaw does not require a plaintiff to prove all three prongs of unfair acts. Rather, "[a] practice may be unfair because of the degree to which it meets one of the criteria or because to a lesser extent it meets all three." Hungate, 139 Hawaiʻi at 411, 391 P.3d at 18 (quoting

Kapunakea Partners v. Equilon Enters., LLC, 679 F. Supp. 2d 1203, 1210 (D. Haw. 2009)).

This conflicts with the federal approach. Congress amended the FTC Act in 1994. Now, plaintiffs suing under the FTC Act *must* prove substantial injury (and more) for an unfair acts claim.[31] See LabMD, Inc. v. Fed. Trade Comm'n, 894 F.3d 1221, 1226 n.10 (11th Cir. 2018) (explaining that "for an act or practice to be unfair, the act or practice [1] causes or is likely to cause substantial injury to consumers [2] which is not reasonably avoidable by consumers themselves and [3] not outweighed by countervailing benefits to consumers or to competition.") (quoting 15 U.S.C. § 45(n)) (cleaned up)).

When interpreting the UDAP, we give "due consideration to the rules, regulations, and decisions of the Federal Trade Commission and the federal courts interpreting section 5(a)(1) of the Federal Trade Commission Act (15 U.S.C. [§] 45(a)(1)), as from time to time amended." HRS § 480-2(b). But no one – not

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[31] 15 U.S.C. § 45(n) (2006) reads:

> The Commission shall have no authority under this section or section 57a of this title to declare unlawful an act or practice on the grounds that such act or practice is unfair unless the act or practice causes or is likely to cause substantial injury to consumers which is not reasonably avoidable by consumers themselves and not outweighed by countervailing benefits to consumers or to competition. In determining whether an act or practice is unfair, the Commission may consider established public policies as evidence to be considered with all other evidence. Such public policy considerations may not serve as a primary basis for such determination.

(Emphases added.)

the State, nor the defendant companies – raised the 1994 FTC Act amendment. (Nor apparently did the parties in our earlier UDAP cases.) Everyone operated under the assumption that the federal changes did not matter, and the State could win without proving substantial injury. This assumption must remain.

We turn to a separate issue that the circuit court spotlighted: an incongruity in this court's treatment of UDAP unfair acts or practices suits.

The circuit court pointed out that despite Hungate's "meets one of the criteria" directive, that case also said "[a] practice is unfair when it [1] offends established public policy and [2] when the practice is immoral, unethical, oppressive, unscrupulous or [3] substantially injurious to consumers." 139 Hawaiʻi at 411, 391 P.3d at 18 (citation omitted) (emphases added). This implied that UDAP plaintiffs must demonstrate public policy plus one of the other elements, while at the same time allowing any one element, alone, to suffice.

We clarify Hawaiʻi's unfair acts or practices UDAP test in one respect: meeting any one of the three criteria supports an unfair acts or practices UDAP claim.

Our approach to unfair acts or practices traces to F.T.C. v. Sperry & Hutchinson Co., 405 U.S. 233 (1972). In Sperry, the Supreme Court ruled that the FTC Act gave the FTC broad powers to determine practices as unfair or deceptive, despite their

effect on competition. Sperry adopted factors the FTC had developed in the cigarette advertising context to determine whether a practice was unfair:

> (1) [W]hether the practice, without necessarily having been previously considered unlawful, offends public policy as it has been established by statutes, the common law, or otherwise—whether, in other words, it is within at least the penumbra of some common-law, statutory, or other established concept of unfairness; (2) whether it is immoral, unethical, oppressive, or unscrupulous; (3) whether it causes substantial injury to consumers . . .

405 U.S. at 244 n.5. Sperry left open what combination of these factors would be sufficient to show unfair acts liability.

In Spiegel, Inc. v. F.T.C., 540 F.2d 287 (7th Cir. 1976), the Seventh Circuit took a "public policy plus" approach to the Sperry factors. It inserted the disjunctive "or" between Sperry's second and third criteria, holding that "A practice is unfair when it offends established public policy and when the practice is immoral, unethical, oppressive, unscrupulous or substantially injurious to consumers." Id. at 293 (emphases added).

Then, in Rosa v. Johnston, 3 Haw. App. 420, 427, 651 P.2d 1228, 1234 (1982), the Intermediate Court of Appeals adopted Spiegel's rearrangement of Sperry. Later, in the context of holding that deceptive and unfair are distinct under UDAP, we mentioned Rosa in passing and said that the ICA "properly" defined unfair acts. Bronster, 82 Hawai'i at 51, 919 P.2d at 313.

But Spiegel's interpretation of Sperry was not the only one. The FTC read Sperry to mean that "[a]ll three criteria do not need to be satisfied to support a finding of unfairness. A practice may be unfair because of the degree to which it meets one of the criteria or because to a lesser extent it meets all three." Promulgation of Trade Regulation Rule and Statement of Basis and Purpose, Disclosure Requirements and Prohibitions Concerning Franchising and Business Opportunity Ventures, 43 Fed. Reg. 59614, 59635 (1978).

The FTC's reading worked for the United States District Court for the District of Hawai'i. Kapunakea, 679 F. Supp. 2d at 1210. Weighing in on HRS § 480-2, the district court referred to Rosa, Bronster, and Spiegel. Id. Then it returned to Sperry, noting that the Sperry test came straight from the FTC and that the FTC in 1978 interpreted the three factors to be disjunctive. The district court followed the FTC's approach.

When we took up the unfair acts issue once more in Hungate, we approved Kapunakea's reasoning: any one of the three criteria could constitute an unfair practice under HRS § 480-2. 139 Hawai'i at 411, 391 P.3d at 18. But Hungate inharmoniously retained the "and-or" language from Spiegel. Hungate didn't clarify whether the appropriate test was fully disjunctive.

We interpret Hawai'i's consumer protection law in a way that maximizes consumer protection. The UDAP "was constructed in

broad language in order to constitute a flexible tool to stop and prevent fraudulent, unfair or deceptive business practices for the protection of both consumers and honest business[people]." Zanakis-Pico v. Cutter Dodge, Inc., 98 Hawai'i 309, 317, 47 P.3d 1222, 1230 (2002) (citation omitted).

The Spiegel approach does not reflect this breadth. We conclude that a disjunctive reading of the Sperry factors best aligns with UDAP's primary purpose - to protect consumers.

Other states have reached the same conclusion. See Cheshire Mortg. Serv., Inc. v. Montes, 612 A.2d 1130, 1143-44 (Conn. 1992) (holding that under Sperry, "[a] practice may be unfair because of the degree to which it meets one of the criteria or because to a lesser extent it meets all three."); see also Robinson v. Toyota Motor Credit Corp., 775 N.E.2d 951, 961 (Ill. 2002) ("[A]ll three of the criteria in Sperry do not need to be satisfied to support a finding of unfairness.").

3. Separate, Independent Grounds for UDAP Liability

Having clarified UDAP unfair acts law, all that remains is to apply it to the present case.

The circuit court determined that the defendant companies' conduct violated each of the three elements for an unfair acts or practices claim. Their conduct: (1) offended public policy; (2) was immoral, unethical, oppressive or unscrupulous; and (3)

substantially injured Hawaiʻi consumers. See Hungate, 139 Hawaiʻi at 411, 391 P.3d at 18.

The court's materiality ruling knocked out its substantially injurious findings. See supra.

That error, however, is not enough for the companies to avoid liability. The court determined that two separate types of unfair acts or practices occurred. The first type focused on the black box label. These findings rely on – and thus were tainted by - the materiality finding. But the second type of conduct – suppressing research and inquiry into the drug for financial reasons – had no connection to the court's materiality ruling. The court's findings about the companies suppressing inquiry into Plavix poor response have nothing to do with the black box label. They have nothing to do with doctors' prescribing habits after 2010. Rather, these findings have everything to do with defendant companies "burying their heads in the sand" over potential issues with a drug on the market.

The court's findings spoke to the other two elements of UDAP unfair acts claims. The court found sufficient facts to support the State's allegation that defendant companies' conduct offended public policy[32] and was unethical.

[32] Defendant companies argue that materiality impacted the court's public policy findings, pointing out that the court said: "Defendants' failure to update the Plavix drug warning after learning of the safety risks posed to poor metabolizers offends this well-established public policy." We agree with Defendants: this finding is only relevant if the black box label matters

First, we turn to the court's public policy findings. Public policy covers a broad range, from state and federal law, to common law, to Hawaiʻi policy. See Hungate, 139 Hawaiʻi at 411, 391 P.3d at 18 ("[a] practice may be unfair if it offends public policy as it has been established by statutes, the common law, or otherwise.") (Cleaned up.)

Pharmaceutical companies have a common law duty to warn consumers "when the risks of a particular drug become apparent." Albrecht, 139 S. Ct. at 1677.

The court-as-factfinder concluded that the companies aimed to avoid their common law duty by: "suppressing research and continuously and repeatedly failing to further investigate the risks of reduced platelet inhibition in poor metabolizers." In its findings, the court determined that the companies knew - from the moment Plavix launched - about the diminished effects of Plavix in non-White populations. It maintained that the companies did not volunteer this information to the FDA. The court further found the companies avoided funding studies which could draw more attention to the variability of response, for instance, by rejecting a study on aspirin resistance because "it could lead to a similar trial on [Plavix] resistance."

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to consumers. The court's materiality ruling foreclosed that evidentiary inquiry.

But the court's reference to the label formed only one part of the court's public policy decision. The other public policy findings had no connection to the black box label or related evidence.

The companies' actions, the court found, set back the research into CYP2C19 by consciously, repeatedly, and actively avoiding the poor responder problem. All this, according to the court, was to avoid "negative marketing implications" for Plavix.

Preventing risks from becoming apparent for financial gain offends Hawaiʻi public policy. Hawaiʻi law cannot incentivize drug companies to ignore safety risks in the hope that everything will turn out all right in the end. Even if the drug proves to be safe, avoiding investigation into known safety issues in order to keep profits up offends public policy. See, e.g., 21 CFR §§ 314.80, 314.81 (requiring a continuing duty of surveillance and post-marketing reporting to the FDA of adverse drug experiences).

The court's findings also animate its determination that the companies behaved in an "immoral, unethical, oppressive, unscrupulous" manner.[33] The court determined that the companies prioritized profits over patients: defendant companies "buried their heads in the sand" about the problems with Plavix to protect the corporate bottom line. The court found the

[33] There is another difference between Hawaiʻi's consumer protection law and federal law. The FTC scrapped Sperry's second criteria long ago. In its 1980 Unfairness Policy Statement, the FTC called the "immoral, unethical, oppressive, unscrupulous" features of an unfair act or practice "largely duplicative." "Conduct that is truly unethical or unscrupulous," the FTC continued, "will almost always injure consumers or violate public policy as well." FTC Policy Statement on Unfairness. https://www.ftc.gov/legal-library/browse/ftc-policy-statement-unfairness [https://perma.cc/3VA6-JMFK].

companies "continued to deny" the issues surrounding poor response to the drug despite evidence to the contrary, giving the impression that no one had any reason to be alarmed. See Hawaii Cmty. Fed. Credit Union v. Keka, 94 Hawaiʻi 213, 229, 11 P.3d 1, 17 (2000) (describing conduct as unethical and unscrupulous when defendant attempted to convince a family to execute loan documents through false assurances about a lower interest rate).

4. No Clear Error in FOFs

The defendant companies argue the court clearly erred in most of the elemental unfair acts and practice factual findings. We disagree.

The trial court fulfilled its duty as fact-finder. See In re ASK, 152 Hawaiʻi 123, 127, 522 P.3d 270, 274 (2022) ("Our view reflects a central feature of any trial: the fact-finder – judge or jury - finds facts, weighs and values those facts, and finds other facts, the facts of consequence."). The court weighed the trial evidence; it drew inferences; it made credibility determinations; it valued some testimony and evidence over other testimony and evidence.

Clearly erroneous facts are either (1) not supported by substantial evidence in the record, Panoke v. Reef Dev. of Hawaii, Inc., 136 Hawaiʻi 448, 460, 363 P.3d 296, 308 (2015) or (2) ones where "despite evidence to support the finding, the

appellate court is left with the definite and firm conviction that a mistake has been committed." Chun v. Bd. of Trs. of the Emps.' Ret. Sys. of the State of Hawai'i, 106 Hawai'i 416, 430, 106 P.3d 339, 353 (2005) (cleaned up). The circuit court's findings do not leave us with either conviction.

The court made sufficient findings of fact that defendant companies' conduct offended public policy and was immoral under UDAP. The substantial injury findings drop because they were affected by the materiality ruling. But the court's findings as to the other two elements are uncoupled from that error. These findings support the court's unfair acts decision. Thus, the court's ruling that Defendants committed unfair acts or practices under UDAP stands.

E. Penalties

Lastly, we turn to the penalties. The defendant companies maintain that the court's materiality ruling impaired its damages calculation. We agree.

We vacate the damage award and remand the penalty issue for determination after the deceptive acts question has been settled.

The court based the penalty for violating UDAP on both deceptive and unfair acts. But now, only the State's unfair acts UDAP violation remains. Any penalty for the deceptive acts claim cannot continue to stand pending a new trial.

We find that the court's heavy reliance on its materiality ruling to reach its penalties determination makes it necessary to remand the entire question of damages. The court reasoned that the $834 million penalty was justified because Defendants had substantially injured the public. Those injuries, the court explained, flowed from the fact that Defendants had denied patients material information. The "injury to the public" paragraph in the court's penalty award discussion uses the word "material" no fewer than three times. The court relied on its materiality findings – and thus the deceptive acts UDAP claim – to calculate its penalty award.

The per-prescription based penalty also shows the circuit court's reliance on the materiality ruling. This type of penalty only makes sense if the missing black box warning was material to consumers. To illustrate this point, the court used the example of hanging an unlawful billboard versus sending thousands of unlawful mailers. For the billboard, an appropriate penalty would count every day the billboard hangs; for the mailers, an appropriate penalty would count every mailer sent. The circuit court thought this case was more like the mailer situation. But this only fits if the omitted information was material to consumers, making it an injury each time they

received the prescription without that information. That is what the new trial will consider.[34]

The claim that Defendants engaged in unfair practices better fits the billboard example. Here, the State's claim focuses on the idea that Defendants suppressed research or failed to sufficiently investigate leads. In these circumstances, an appropriate penalty would correlate more with the length of time the Defendants "buried their heads in the sand."

That the court landed on a per-prescription penalty reveals how crucial materiality was to the damage calculations.

Because the penalty award relied on the court's faulty materiality ruling, it must be vacated. Only the claim that Defendants committed unfair acts or practices in violation of UDAP remains. At the new trial, it may be that Defendants will be found to have committed deceptive acts as well, or found to have only committed unfair practices. The nature of the UDAP violation will determine the proper penalty for that violation. Since the final penalty will be partially contingent on the result, the penalty determination should take place after the new trial, by the judge who conducts that trial.

[34] We are unpersuaded by the defendant companies' arguments regarding "coercive" and "biased" treatment by the trial court. This case, however, is remanded to a new trial judge.

IV. CONCLUSION

We vacate the circuit court's grant of partial summary judgment on materiality, the court's deceptive acts holding, and its penalty award. The court's unfair acts holding stands. We remand only as to the deceptive acts and penalty issues.

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/s/ Paula A. Nakayama

/s/ Sabrina S. McKenna

/s/ Todd W. Eddins

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