**FALSE CLAIMS ACTIONS BASED ON THE OFF-LABEL MARKETING OF DRUGS:**

**A COMPARISON OF *KING, D’AGOSTINO, CAMPIE,* AND *BROWN***

Robert Vogel

Sylvia Pap

Vogel, Slade & Goldstein, LLP

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The Food, Drug and Cosmetic Act (“FDCA”) forbids pharmaceutical manufacturers from marketing or selling a drug until the Food and Drug Administration (“FDA”) has approved it as safe and effective for its intended use or uses (the drug's “indications”). *See* 21 U.S.C. §§ 355(a), (d). An *unapproved* use of an FDA-approved drug is referred to as “off-label.”[[1]](#footnote-1) This can include the use of a drug for a disease or condition that the drug was not approved to treat, or administration of the drug in a different way or form from what was approved, or even an unapproved dosage of the drug. FDA generally does not restrict physicians from prescribing an otherwise FDA-approved drug for an off-label use. *See* 21 C.F.R. §312.3(d) (exemption from FDA regulations for “the use in the practice of medicine for an unlabeled indication of a new drug product approved” by FDA); *see* *also* 21 U.S.C. § 396 (“Nothing in this chapter shall be construed to limit or interfere with the authority of a health care practitioner to prescribe or administer any legally marketed device to a patient for any condition or disease within a legitimate health care practitioner-patient relationship.”).

Demonstrating False Claims Act liability resulting from the marketing of prescription medications for off-label uses has proven difficult for a number of reasons, as seen in recent cases such as *United States ex rel. King v. Solvay Pharmaceuticals,* 871 F.3d 318 (5th Cir. 2017) (“*King*”) and *D'Agostino v. ev3, Inc.*, 845 F.3d 1 (1st Cir. 2016) (“*D'Agostino”*). By contrast, in two cases where courts have allowed plaintiffs to proceed on theories that defendants violated the FCA by causing the submission of claims for reimbursement for drugs that were marketed off label,, *United States ex rel. Campie v. Gilead Sciences, Inc.,* 862 F.3d 890 (9th Cir. 2017) (“*Campie*”) and *United States ex rel. Brown v. Celgene Corporation,* 226 F.Supp.3d 1032 (C.D. Cal. Dec. 28, 2016) (“*Brown*”), the plaintiffs were able to allege or present overwhelming evidence that defendants were systemically marketing drugs in clear violation of FDA regulations. This paper will address these four cases.

# ***King***

In *King,* the Fifth Circuit upheld the district court’s grant for summary judgment to defendant Solvay Pharmaceuticals, Incorporated (“SPI”). The relators, John King and Tammy Drummond, brought a False Claims Act action against pharmaceutical manufacturer SPI, alleging that it caused the submission of false Medicaid claims through a nationwide off-label marketing and kickback scheme to promote three drugs: Luvox, Aceon, and AndroGel. Relators were formerly employed by SPI as District Sales Managers and had their employment terminated for raising questions about SPI marketing practices in 2002, respectively. Relators initially filed their *qui tam* lawsuit (under seal) in June 2003 on behalf of the United States and various states. Relators’ second amended complaint was unsealed in December 2009. Ultimately, relators sought to amend their complaint five times.

Relators alleged several FCA violations against SPI linking their off-label marketing of the drugs and the actual filing of false claims. Relators alleged that (1) SPI’s marketing of the drugs caused physicians to prescribe them to Medicaid patients for off-label uses, (2) SPI lobbied members of state pharmaceutical and therapeutic committees to include the drugs on their preferred drug lists, (3) SPI used misleading information to lobby the publisher of drug compendium DRUGDEX Information System (“DrugDex”), and (4) SPI paid physicians kickbacks to prescribe these drugs to Medicaid patients. Relators also brought an FCA retaliation claim challenging their terminations.

Relators contended that SPI marketed Luvox, a selective serotonin reuptake inhibitor (SSRI), for use in treating depression, anxiety-related disorders, and other conditions on what SPI called the “OC Spectrum,” even though Luvox was not specifically approved for these conditions. Relators pointed to specific physicians in Texas who prescribed Luvox for off-label uses after sales representatives “pitched” these uses during sales calls. *United States ex rel. King, et al., v. Solvay, et al., ,* 823 F.Supp.2d 472, 483 (S.D. Texas 2011). Relators contended that Solvay also engaged in off-label marketing of Aceon, a medication that was approved for the treatment of high blood pressure, by pitching that medication in marketing talks to physicians, encouraging the physicians to prescribe the drug for patients with diabetes or cerebrovascular disease. Finally, relators alleged that Solvay marketed its product AndroGel, which was approved to treat testosterone deficiencies, to Texas physicians for the treatment of various other conditions. *Id*. at 483-84. Relators contended that the off-label promotion of Luvox, Aceon, and AndroGel resulted in the submission of false claims to government health care plans, including Medicare, Medicaid, and TRICARE. Relators also asserted that Solvay's drugs were added to Medicare and Medicaid formularies after listings in DRUGDEX Information System supported the off-label uses, even though FDA specifically denied approval for some of the off-label uses listed, and many of the sources cited in DRUGDEX in support of the off-label uses were questionable. Relators claim that DRUGDEX listed the uses because of false or misleading statements by Solvay. *Id*. at 484.

The district court for the Southern District of Texas disposed of all of the Relators’ claims through a series of partial summary judgment orders, holding that the court lacked jurisdiction over certain claims under the FCA’s public disclosure bar, rejecting some of Relator’s evidence as inadmissible, and rejecting other claims on the grounds that the Relators had failed to introduce sufficient evidence of causation.

On appeal, the Fifth Circuit affirmed the grant of summary judgment to SPI on all the Relators’ claims. Most significantly, the court of appeals emphasized the lack of evidence that the defendant’s off-label marketing activities had caused the submission of false claims to Medicaid for the off-label use of the drugs. Pointing to the language of 21 U.S.C. § 396, the court noted that “the FDA does not restrict physicians from prescribing an otherwise FDA-approved drug for an off-label use.” *United States ex rel. King, et al., v. Solvay Pharmaceuticals, Inc.*, 871 F.3d at 328.

In support of their position, Relators referred to an expert report claiming that economic studies showed a link between pharmaceutical marketing and increased pharmaceutical sales. Relators argued that this demonstrated that Solvay’s off-label marketing scheme must have resulted in an increase in the number of off-label prescriptions that were reimbursed through the Medicaid program. The court rejected this conclusion as speculative and therefore insufficient to preclude summary judgment. The court concluded that, despite Relator’s attempt to show a correlation between marketing and prescribing, “without evidence indicating that off-label marketing actually caused off-label prescriptions to Medicaid patients resulting in false claims to the government, Relators’ off-label marketing theory of FCA liability cannot survive summary judgment” *Id.* at 329.

Relators also argued that causation could be established from a set of call notes recorded by sales representatives about their communications with physicians regarding Luvox and Aceon. The court rejected that argument, finding that most of the call notes did not discuss specific off-label use, and the ones that did only showed physicians explaining their practices, “which provides no insight into whether Solvay marketed the off-label uses to them, let alone caused them to make off-label prescriptions.” *Id.* Relators argued that physicians may have been influenced by academic articles discussed in those calls, but the court found no evidence that physicians knew about the articles as a direct result of communications from SPI or its sales representatives. The court concluded, “the probative value of Relators' causation evidence is primarily based on conjecture and speculation and is therefore insufficient to create a genuine issue of material fact for trial.” *Id.*

# ***D’Agostino***

In *D’Agostino*, the First Circuit affirmed dismissal of a case filed against ev3, Inc. (“ev3”) and its subsidiary, Micro Therapeutics (“MTI”). Ev3 and MTI manufactured and sold a medical device, Onyx, that was designed to minimize blood loss to reduce the BAVM size prior to brain surgery. *D’Agostino,* 845 F.3d at 4. In its application to FDA for pre-market approval of Onyx, MTI emphasized that physicians would be required to undergo a rigorous training program prior to using the device. FDA’s advisory panel recommended approval of Onyx, but in doing so, it emphasized that these training requirements were “‘critically important’” and ‘a very big component of getting [Onyx] into safe use.’” *Id.* (citation omitted). The FDA granted approval to Onyx in July 2005, but the label restricted use to “’physicians with neurointerventional training and a thorough knowledge of the pathology to be treated, angiographic techniques, and super-selective embolization.’” *Id.* (citation omitted).

D'Agostino was hired as an ev3 sales representative in January 2005 until his termination in January 2010. He claimed that, contrary to MTI’s representations that it would require physicians to undergo extensive training prior to using Onyx, the FDA-mandated physician trainings for Onyx were as short as four hours long and discussed surgeries that used off-label procedures, and the company would sell Onyx to any site where a single neurosurgeon who had completed their training. As a result, D’Agostino alleged, physicians “with inadequate training or no training at all” were using Onyx, in violation of the FDA-approved label. *Id.* D’Agostino also contended that the defendants encouraged off-label marketing by setting sales quotas, educating on “‘peripheral applications,’” and training physicians during paid retreats. *Id.* (citation omitted).

Ev3 launched another product, Axium, in 2007 after clinical trials indicated numerous problems with Onyx in treating aneurysms. The defendants redesigned the device several times in response to persistent malfunction reports, but they did not recall or relabel earlier models. D'Agostino attended a February 2009 meeting where organization leaders urged the sales force to ignore these and other defects in order to avoid FDA inspection.

Approximately one year after the February 2009 meeting, ev3 terminated D’Agostino’s employment. In October 2010, he filed a *qui tam* action under seal in the United States District Court for the District of Massachusetts. In October 2013, the United States declined to intervene, and the court lifted the seal. D’Agostino ultimately sought leave to file a fourth amended complaint, but the district court found the motion to be futile and dismissed the lawsuit. D’Agostino filed an appeal to the First Circuit.

Before the district court and the First Circuit, D’Agostino contended that the Onyx device label required use by “trained physicians,” and therefore, the “use by untrained physicians was both off-label and … not medically necessary.” *Id.* at 11. The First Circuit rejected this argument, finding that the label did not require that MTI or ev3 provide the training, and that the allegations that the defendants did not train physicians therefore fell “materially short of alleging facts showing that they were not trained *at all*.” *Id.* (emphasis added).

The First Circuit also found that D’Agostino’s off-label marketing claim would fail for an additional reason: he assumed that, because the allegedly untrained physicians treated many patients who were insured under government programs, the physicians must have been submitting claims for services rendered to those patients. The court found that this assumption was not supported by evidence that the physicians who lacked training actually submitted claims for government reimbursement for performing procedures involving the device on these patients.

# ***Campie***

Whereas off-label use normally pertains to cases of a FDA-approved drug being prescribed for a non-approved use, *Campie* involves allegations that several anti-HIV drugs were approved on the basis of false representations by the manufacturer to FDA. Relators Jeff and Sherilyn Campie alleged that the defendant, Gilead, violated the False Claims Act by knowingly causing the submission of claims for reimbursement of adulterated drugs, *i.e.*, drugs that were materially different from forms that had been approved.

Gilead manufacturers several anti-HIV drug therapies, including Atripla, Truvada, and Emtriva. Relators claimed that in 2008 and 2009, the government paid over $5 billion to Gilead for these drugs, and that during this period, the defendant concealed from FDA that it was manufacturing the drugs in violation of FDA-approved processes. Relators further claimed that Gilead made false statements regarding their compliance with FDA requirements.

Gilead’s anti- HIV drugs Emtriva, Truvada, and Atripla contain the active ingredient emtricitabine (commonly known as “FTC”). In applying for FDA approval for these drugs, Gilead represented that it would obtain the FTC from specific registered facilities. Relators alleged, however, that in 2006, Gilead attempted to save money by contracting with Synthetics China for unapproved FTC at unregistered facilities, and that Gilead falsely represented that the FTC had come from an approved South Korean company. Gilead eventually sought approval from FDA to use Synthetics China’s FTC in October 2008, and FDA ultimately granted the approval in 2010. The relators alleged that Gilead had been producing the adulterated products for at least two years prior to obtaining FDA’s approval in 2010, and that during this interim time period, Gilead was concealing data in its FDA application and was importing FTC with fraudulent labeling.

The relators filed a *qui tam* case, and the United States declined to intervene. The district court dismissed the case for failure to state a claim under Fed.R.Civ.P. 12(b)(6), and relators appealed the dismissal to the Ninth Circuit. The Ninth Circuit reversed the district court, holding that the Relators’ complaint set forth various claims for relief under the False Claims Act.

The court first resolved the question of whether the Relators sufficiently alleged that the defendant’s conduct resulted in the submissions of claims that were “false,” holding:

Here, relators allege false statements permeating the regulatory process. They allege Gilead mislabeled and misbranded nonconforming drugs and misrepresented its compliance with FDA regulations by omitting critical information. They allege that Gilead established policies and practices to violate the FDA’s regulatory requirements and allege specific instances of such violations, such as altering inventory codes, and mislabeling or altering shipping and tracking information. All the while, Gilead was submitting claims for payment for “FDA approved” drugs. Moreover, they allege that Gilead made false statements regarding test results in order to get FDA approval and thus become eligible for government funds. … Relators adequately plead falsity under the False Claims Act. To hold otherwise would reduce FDA regulations akin to approval of the curate’s egg.

862 F.3d at 904.

The *Campie* court then turned to the question of whether the defendant’s false statements and claims were “material,” under the standards set forth in the Supreme Court’s decision in *Universal Health Servs., Inc. v. United States*, 136 S.Ct. 1989 (2016). The *Campie* court acknowledged: “It is undisputed that at all times relevant, the drugs at issue were FDA-approved, and that the government continues to make direct payments and provide reimbursements for the sale of the three drugs. Relators thus face an uphill battle in alleging materiality sufficient to maintain their claims.” *Id*. 862 F.3d at 905. The court found, nonetheless, that the relators had alleged enough to survive a motion to dismiss their complaint. The court held:

Relators and the United States persuasively argue, however, that to read too much into the FDA’s continued approval—and its effect on the government’s payment decision—would be a mistake. First, to do so would allow Gilead to use the allegedly fraudulently-obtained FDA approval as a shield against liability for fraud. Second, as argued by Gilead itself, there are many reasons the FDA may choose not to withdraw a drug approval, unrelated to the concern that the government paid out billions of dollars for nonconforming and adulterated drugs. Third, … Gilead ultimately stopped using FTC from Synthetics China. Once the unapproved and contaminated drugs were no longer being used, the government’s decision to keep paying for compliant drugs does not have the same significance as if the government continued to pay despite continued noncompliance.

*Id*. at 906. Finding that it lacked evidence as to “exactly what the government knew and when, calling into question its ‘actual knowledge,’” the court concluded, “The issues raised by the parties here are matters of proof, not legal grounds to dismiss relators’ complaint.” *Id*.

The court took into consideration several other cases, including *D’Agostino*, in which courts of appeals had rejected theories of False Claims Act liability based on off-label marketing. The court distinguished those cases, saying:

We note that other courts have cautioned against allowing claims under the False Claims Act to wade into the FDA’s regulatory regime. … However, just as it is not the purpose of the False Claims Act to ensure regulatory compliance, it is not the FDA’s purpose to prevent fraud on the government’s fisc. Mere FDA approval cannot preclude False Claims Act liability, especially where, as here, the alleged false claims procured certain approvals in the first instance.

*Id*. at 905 (citations omitted).

# ***Brown***

In *Brown*, the pharmaceutical manufacturer Celgene Corp. agreed to pay $280 million in July 2017 to settle fraud allegations for the off-label promotion of two drugs for cancer treatment, uses which had not approved by the FDA.[[2]](#footnote-2) This followed the defendant’s motion for summary judgment on all claims asserted by the relator, Beverly Brown (“Brown”). Brown filed her *qui tam* suit in 2010, alleging, among other things, that Celgene violated the False Claims Act by engaging in an unlawful campaign to promote the drugs Thalomid and Revlimid for off-label use in the treatment of cancer patients.

Thalomid received FDA approval in July 1998 for the treatment of a complication associated with leprosy; later, in May 2006, the drug was approved for the treatment of multiple myeloma (“MM”), a form of cancer. Revlimid first received FDA approval in December 2005 for “the treatment of patients with transfusion dependent anemia,” and then in June 2006 for MM patients. In June 2013, the FDA also approved Revlimid for the treatment of mantle cell lymphoma patients “whose disease has relapsed or progressed after two prior therapies, one of which included bortzezombid.” 226 F.Supp.3d at 1035.

Brown was hired by Celgene in April 2001 as an “Immunology Specialist,” although she actually performed sales work. In 2007, Brown became concerned when her manager instructed her to call physicians' offices to ask them to change billing codes associated with prescriptions of Celgene drugs. Brown sent a letter to management complaining about this practice, and she later contacted the FDA and legal counsel. In April 2010, Brown, acting on behalf of the United States as well as various states and other government entities, initiated this *qui tam* action against Celgene. These governmental entities all declined to intervene. The case was unsealed, and the complaint was served in October 2013. In August 2016, Celgene moved for summary judgment.

According to Brown, Celgene's off-label promotion mostly involved direct contact with physicians and was centered on the treatment of cancer patients. Although Celgene's drugs were not approved for any cancer use until 2005 and were only approved for a narrow subset of cancers thereafter, the company began promoting Thalomid and Revlimid for a wide variety of cancers as soon as these drugs hit the market. Brown also alleged that Celgene paid kickbacks in the form of speaker fees, paid clinical trials, advisory board positions, and authorship of ghost-written articles to physicians in exchange for prescriptions of its drugs. Celgene's efforts were successful in causing physicians to prescribe Thalomid and Revlimid, and many of the resulting prescriptions were reimbursed by Medicare, Medicaid, TRICARE, and the Department of Veterans Affairs (“VA”).

To defeat the motion for summary judgment, Brown had to demonstrate a causal link between Celgene’s off-label marketing efforts and the actual prescription of drugs for off-label purposes, and more specifically, prescriptions of drugs that were billed to Medicare for reimbursement. Celgene argued that truthful off-label promotion may be protected by the First Amendment, and that these health programs have discretion to reimburse off-label uses that are in a patient's best interest. Celgene cited clinical research and medical expert acknowledgement of the potential effectiveness of Thalomid and Revlimid in treating cancer, as well as declarations from physicians about exercising independent judgment in prescriptions. This evidence, which tended to negate any causal link between drug promotion and drug prescription, left the burden on Brown to produce evidence from which a reasonable jury could infer such a causal link. *See id.* at 1037.

Brown, however, was able to produce such evidence. First, she pointed to the timing and limited scope and of FDA’s initial approvals of Thalomid and Revlimid. Thalomid had not been approved to treat any kind of cancer until May 2006, and it was originally approved only to treat a condition that results from leprosy and occurs in about a quarter of the “few hundred” cases diagnosed each year. *Id.* Revlimid was not approved at all until December 2005, then was approved for the treatment of MM in 2006, and its approval was limited to uses “similarly narrow in scope.” *Id.* at 1038. Based on these facts, the court declared, “Celgene arguably should not have promoted its drugs to treat cancer before December 2005; even after this point, its promotion arguably should have been limited to the narrow subset of cases for which it had received approval.” *Id.*

Brown provided evidence showing that Celgene had begun marketing Thalomid for off-label cancer uses almost as soon as it gained approval for ENL in 1999. Celgene had devised a “Thalomid Marketing Plan,” which included sales materials for doctors, exhibits at conventions, and advertisements in medical journals focused on physicians who specialize in cancer. A 2004 Business Plan “urged representatives to discuss off-label cancer uses ‘on every call’” *Id.* Brown was able to provide first-hand evidence of Celgene’s practices: she herself had been a sales representative, hired in 2001, trained, and instructed to discuss off-label uses of Thalomid for cancer patients with oncologists and hematologists. Brown provided evidence that the sales force for Thalomid started with about 20 people at the launch of the drug, and then grew to more than 230 people in 2006, and that these sales representatives regularly discussed off-label use with physicians. *Id.* at 1039.

To buttress her claim on the element of causation, Brown provided expert analysis of sales contacts made by Celgene's sales representatives between August 2004 and May 2006. Celgene's sales representatives made 4,000-5,000 contacts per month, with almost 80% of these contacts involving hematology or oncology, and sold between 800,000 and 1,000,000 Thalomid capsules per month, with 99.75% of sales between 2001 and 2005 for off-label uses. The expert concluded that those who received more promotional contacts prescribed at a higher rate than those who received fewer.

It is noteworthy that Brown’s evidence on causation appears to have been far more detailed and specific than the general economic study of correlation between marketing and prescribing produced by the relators in *King.* Moreover, unlike the relator in *King*, who could point only to a few specific examples of off-label prescribing by doctors in Texas, Brown introduced evidence of the widespread submission of off-label claims for Thalomid and Revlimid. Indeed, Brown’s expert witness estimated that approximately 43,092 claims for off-label use of Thalomid presented to Medicare between 1999 and 2005, and another 133,854 claims for off-label uses of Thalomid and 152,060 claims for off-label uses of Revlimid after 2005. Based on this evidence, the district judge concluded:

Brown's evidence shows that Celgene engaged in a systematic campaign to promote off-label uses of Thalomid and Revlimid, that physicians who received more promotional contacts prescribed at a higher rate than those who received fewer contacts, that Celgene knew its promotional activities were delivering results, and that marketing to doctors is generally effective.

*Id.* at 1040.

After determining that Brown had sufficient evidence of causation, the district judge focused on the question of materiality. Brown contended that the claims for off-label prescriptions of Thalomid and Revlimid were false because providers failed to disclose that the claims were not for medically accepted indications. The court found that Medicare Part D may only reimburse covered drugs which must be “used for a medically accepted indication.” *Id*. at 1049 (quoting 42 C.F.R. § 423.100). The district court acknowledged that while this coverage limitation was not “automatically dispositive” of the materiality inquiry, it was highly relevant. *Id*. Finding that coverage limitations are an “essential feature” of the Medicare Part D Program, the court concluded: “*Escobar* does not foreclose the possibility that a statutory requirement may be so central to the functioning of a government program that noncompliance is material as a matter of law” *Id.*

Celgene argued that its off-label marketing could not be material, claiming that the Government had “actual knowledge” of the alleged violations, yet continued to pay the disputed claims. Celgene contended that from the time Thalomid and Revlimid had first been approved, FDA was aware that they were being used off-label – and, indeed, Celegene itself had submitted reports to the FDA disclosing off-label uses of those drugs. The court rejected this argument, holding: “The fact that the FDA knew generally about off-label use does not mean CMS knew about and agreed to reimburse particular off-label claims.” Id. at 1050. Celegene further argued that CMS continued to pay claims for off-label uses of the drugs even after Brown filed her *qui tam* case in 2010. *Id*. Also rejected this argument, the court held: “Even if CMS knew after 2010 that incoming claims for Thalomid and Revlimid included claims that failed to meet the medical acceptance requirement, it does not follow that CMS had actual knowledge that particular claims were non-compliant and reimbursed them anyway. This evidence does not establish non-materiality as a matter of law.” *Id*. at 1050-51. The court concluded, “Celgene has not shown that it is entitled to summary judgment on materiality grounds.” *Id*. at 1051.

# ***Conclusion***

Each of the four cases discussed herein involve somewhat different fact patterns. In *D’Agostino*, the court of appeals affirmed the dismissal of the relator’s off-label claims on the grounds that the relator had not sufficiently alleged an off-label use of the products: although the relator alleged that the defendants failed to train physicians in accordance with the labelling requirement, the label did not strictly require that the defendants personally perform such training. In *Campie*, the relator’s claim was not that the defendant was promoting an approved drug for off-label uses, but rather, that the defendant was producing and distributing adulterated products, *i.e.*, products that were not the same as what FDA had approved.

The two cases that bear the closest resemblance to each other were *King* and *Brown*, insofar as both cases involved well-pleaded allegations that the defendants were promoting drugs for off-label use, but the question was whether the relators could also adequately plead that the defendants were submitting or causing the submission of false claims for reimbursement. The different outcomes in the two cases could be explained by the difference in the strength of the evidence supporting a causal connection between the defendants’ off-label marketing activities and the doctors’ prescribing decisions. In *King*, the relator came forward with only tenuous evidence of such a connection – namely, evidence of off-label marketing activities, an expert report describing the general connection between marketing efforts and prescription patterns, and a few examples of off-label prescriptions within a limited geographic territory. Conversely, in *Brown*, the relator was able to provide extensive research, specific data, and personal experience demonstrating that Celgene’s marketing efforts centered on promoting the off-label use of its products, and that Celgene had been wildly successful in promoting massive off-label use.

1. https://www.fda.gov/ForPatients/Other/OffLabel/ucm20041767.htm [↑](#footnote-ref-1)
2. https://www.justice.gov/usao-cdca/pr/celgene-agrees-pay-280-million-resolve-fraud-allegations-related-promotion-cancer-drugs [↑](#footnote-ref-2)