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# The Double-Edged Effect of First Amendment Factors On the Government Approach to Off-Label Enforcement: Interpreting Recent Government Statements

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## *Introduction*

In the past few years, developments in First Amendment case law, notably the Second Circuit's decision in *U.S. v. Caronia*,[1] raised hopes among those who believe that criminal prosecutions and civil claims based on truthful speech about drugs and medical devices are unconstitutional. But of course, by declining to seek *certiorari* in *Caronia*, the government deprived the Supreme Court of the opportunity to adopt or expand on *Caronia's* reasoning and apply it nationwide; and even within the Second Circuit, in crucial ways the full implications of *Caronia* remain unclear.

Against this backdrop, recent remarks by Assistant Attorney General Stuart Delery at the CBI Congress[2] appear to confirm that the prospect of greater protection for truthful off-label speech has not diminished the government's determination to bring enforcement actions against off-label promotion – even where it may not be false or misleading. Similarly, the recently issued FDA Draft Guidance on the distribution of scientific publications[3] (''Draft Guidance'') also shows that the government continues to regard the prohibition of off-label speech, including speech that is not necessarily either false or misleading, as an essential tool in the protection of public health.

AAG Delery's remarks suggest that, at least for now, the DOJ may deal with First Amendment concerns not by foregoing cases based on truthful scientific speech, but rather by framing those cases as aimed at unlawful conduct (the distribution of a product for an unapproved ''intended use'') and contending that the First Amendment permits the use of speech as evidence of the intended use for which the product is distributed. This is essentially the same argument the government made in *Caronia*, an argument the Second Circuit rejected because the record showed that the Caronia's conviction was based directly and solely on speech. 703 F.3d at 160-62. To avoid a similar result in future cases, the government is likely to do more than it did in Caronia to try to show that its target is unlawful conduct and intent, not just off-label communications.

Assuming the government does attempt to position future cases more convincingly as aimed at conduct not speech, it is likely to rely more than ever on evidence other than actual promotional speech in building and bringing cases; and it might even be disposed to bring cases based solely, or at least primarily, on evidence

[1] 703 F.3d 149 (2d Cir. 2012) (10 PLIR 1525, 12/7/12).

[2] Assistant Attorney General Stuart F. Delery Delivers the Keynote Address at the CBI Pharmaceutical Compliance Congress, Jan. 29, 2014. Text at http://www.justice.gov/iso/opa/civil/speeches/2014/civ-speech-140129.html.

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[3] Distributing Scientific and Medical Publications on Unapproved New Uses – Recommended Practices, February 2014, http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM387652.pdf (12 PLIR 307, 3/7/14).

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other than external, promotional communications. As a consequence, even if their promotional review and compliance practices ensure that such communications are strictly on label, manufacturers may have to be more concerned than ever that the government will see evidence of wrongdoing elsewhere – for example, in the mere distribution of products that are widely used off label, or in internal documents that discuss off-label use and sales. Perversely, at least in the short run, the prospect of tougher First Amendment scrutiny may have enlarged rather than restricted the range of communications and conduct on which the government might choose to base enforcement actions.

## *The Government's Continuing Reliance on a ''Conduct'' Theory of Liability for Off-Label Speech*

AAG Delery's January 29 remarks indicate that the government continues to regard truthful speech as fair game for enforcement action. While acknowledging the benefits of ''open dialogue'' in which ''companies and physicians share truthful information about a product[ ],'' he emphasized that the government would ''act aggressively'' wherever a manufacturer ''crosses the line and distributes its products intending them to be used'' for unapproved indications. Conspicuously, in promising aggressive action against any company that ''crosses the line,'' the AAG did *not* say that the line was between truth and falsehood.[4] A manufacturer can be targeted for enforcement if it distributes a product with the necessary intent, with or without any false or misleading off-label communications — indeed, theoretically, without any actual off-label communications at all.[5]

Similarly, under the FDA's recent Draft Guidance, as under previous similar guidelines, for a manufacturer to be allowed to distribute a scientific publication, it is not enough for it to be truthful and non-misleading, the publication must also fulfill an assortment of additional criteria demonstrating the independence of the author and publisher and the absence of manufacturer influence over content. Like AAG Delery's remarks, the Draft Guidance purports to focus primarily on the ''intended use'' of a drug, and considers under what circumstances the distribution of scientific materials by a manufacturer may be considered evidence of such ''intended use.''[6]

In their focus on manufacturer intent, and on conduct rather than speech, AAG Delery's remarks and the Draft Guidance are predictably consistent with longstanding government theories of liability for off-label promotion. Because the Food, Drug and Cosmetic Act does not ban off-label speech as such, off-label promotion has been prosecuted as ''misbranding'' on the theory that a product promoted for off-label use is ''misbranded'' because it lacks ''adequate directions for use'' to the extent that its ''intended use'' is off-label.[7] Alternatively, in the government's view, the promotion of a drug for an unapproved ''intended use'' also violates the drug approval requirements of the FDCA because the product is an unapproved new drug with respect to that off-label use. *See, e.g.*, Brief for United States of America, Appellee, *Caronia*, Nos. 09-5006, 10-0750, 2010 WL 6351497, at *61 (2d Cir. Oct. 8, 2010) (citing 21 U.S.C. §§ 331(d) and 355(a)). *See also* Draft Guidance at 4 (stating that an approved drug accompanied by written matter suggesting an unapproved use may be an ''unapproved new drug'' for that use, and that an approved drug ''intended for'' an unapproved use ''whether referenced in the labeling or not,'' would be misbranded because it does not bear adequate directions for use). Both these theories purportedly base liability on conduct and intent rather than speech as such, and the government has argued that because it does not prosecute speech directly, it may offer speech as evidence of intent without violating the First Amendment.

This theory that truthful speech may properly be targeted as evidence of intended use was at issue in *Caronia*. The government asserted that Caronia was prosecuted not for his truthful speech but rather for his involvement in unlawful conduct—distributing a misbranded drug—with speech used only as evidence of the unapproved intended use for which the drug was distributed. 703 F.3d at 160-62. The Second Circuit rejected the argument, but not categorically. The Court of Appeals held that at least in Caronia's particular case, the government had prosecuted the defendant for his speech, and his conviction was based upon it. *Id.* But Caronia did not completely rule out the possibility that a prosecution more convincingly presented as targeting conduct and intent could survive First Amendment scrutiny[8] ; and in declining to seek further review of the

[4] To the extent that the AAG alluded to any factors that might conceivably drive the government's decisions about which off-label cases to pursue, he focused on the asserted harm to patients from unapproved uses – not truth or falsehood; and while truthful off-label promotion might reasonably be assumed to be less potentially harmful to patients than false or misleading promotion, there's no reason to believe that the government would for that reason rule out pursuing cases based on truthful speech.

[5] Even to the extent that the government might limit off-label enforcement actions to cases involving what it considers to be false or misleading communications, its operative definition of ''false or misleading'' would likely include any statements not supported by evidence up to the FDA's rigorous standards, including for example those listed in 21 CFR 202.1(e)(6). Interestingly, in this area, another Second Circuit Case, *ONY, Inc. v. Cornerstone Therapeutics, Inc.*, 720 F.3d 490 (2d Cir. 2013), (a Lanham Act case involving private parties) may have cast at least some doubt upon the government's ability to bring cases based on scientific conclusions and analyses in areas of legitimate debate.

[6] Interestingly, although it reviews the First Amendment case law surrounding the distribution of scientific and medical publications, and although it discusses the background of the government's off-label enforcement authority, the Draft Guidance does not contain any reference to *Caronia*.

[7] *See Caronia*, 703 F.3d at 154 (''A drug is misbranded if, *inter alia*, its labeling fails to bear 'adequate directions for use,' 21 U.S.C. § 352(f), which FDA regulations define as 'directions under which the lay[person] can use a drug safely and for the purposes for which it is intended,' 21 C.F.R. § 201.5. FDA regulations define intended use by reference to 'the objective intent of the persons legally responsible for the labeling of drugs . . . .' '')

[8] The court assumed without deciding that the evidentiary use of speech to prove intended use might be permissible. 703 F.3d at 162 n.9. It did however express doubts about how such use might work. *Id.* And at least some language in *Caronia* does suggest that the court viewed the government's whole theory of liability for off-label promotion, not just its prosecu-

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decision, the government specifically noted that *Caronia* ''did not address the constitutionality of the theory of liability'' on which the government had defended the conviction.[9]

As Caronia's counsel argued, at least in the misbranding context, targeting truthful speech as ''evidence'' may very well violate the First Amendment just as surely as targeting it directly. Appellant's Reply Brief, *Caronia*, Nos. 09-5006-cr(L), 10-0750(CON), 2010 WL 6351498, at *11-17 (2d Cir. Nov. 4, 2010). To the extent that the intended use for which a manufacturer sells an allegedly misbranded drug can be determined only on the basis of its communications, any prosecution for such misbranding is effectively based solely on speech; and if that speech cannot be shown to be false or misleading, the prosecution arguably violates the First Amendment.

That said of course, even if *Caronia* did cast serious doubt on the government's rationale for prosecuting truthful speech, as long as the government *thinks* it can bring cases based on such speech, manufacturers must and will inevitably act as though it can – complying with the law as the government interprets it, and wary of the extreme risks involved in putting the government's theories to the test of litigation.

## *Implications of the Focus on Conduct and Intent in Off-Label Cases*

The mere fact that the government still believes it can bring cases based on truthful off-label speech is not surprising. The government has never conceded that it could not. The more interesting issue raised by AAG Delery's remarks is how the government's reliance on the speech/conduct dichotomy to insulate its claims from First Amendment scrutiny may affect the way it constructs cases. If the government believes that off-label cases must be built on conduct and intent in addition to (or even instead of) speech, how might that view affect the way in which it investigates and evaluates evidence?

It would be unwise to try to base detailed analyses or predictions on a few passages from a brief speech by the AAG, or on FDA guidance on the single issue of scientific publications; but some likely possibilities come to mind. First, to present its cases as based on conduct and intent rather than speech, the government is likely to focus more attention than ever on evidence other than external, promotional speech about a manufacturer's products. Internal communications, such as business and strategic plans discussing off-label use and potential new indications, have always been important in cases against drug and device companies. They may now be perceived as critical support for a successful case.

In addition, as AAG Delery's remarks appear to illustrate, in emphasizing conduct as opposed to speech the government may be more disposed to treat the mere distribution of a product known to be widely used off label as evidence of a misbranding violation. In describing the alleged conduct underlying Johnson & Johnson's recent settlement with the government relating to the antipsychotic drug Risperdal, the AAG said that Janssen (the J&J subsidiary that sold the drug) ''distributed the drug to health care providers for elderly, non-schizophrenic dementia patients'' for unapproved uses ''despite knowing that those uses were not approved.'' Similarly, as already noted, the AAG emphasized that a manufacturer could ''cross[ ] the line'' into misconduct by ''distribut[ing] its products intending them to be used'' in unapproved ways. His emphasis on ''distribution'' rather than promotion or other communication suggests that the government may, more than ever, seek to use distribution with knowledge of off-label use as evidence of the intended use on which to base a misbranding charge.

First Amendment considerations may thus incline the government to treat non-promotional evidence as essential to a successful case. But perhaps even more notably, in focusing more rigorously on conduct and intent, the government may be disposed to bring cases based entirely, or at least primarily, on such evidence; and it may be more willing than ever to take action even where evidence of actual off-label communications might be thin or ambiguous.

The idea that an ''intended use'' of a product may be inferred not just from actual expressions but also from the mere sale of the product with knowledge of that use is highly problematic. In CFR 201.128, ''intended uses'' are defined in terms of the ''*objective intent* of the persons legally responsible for [labeling]'' (emphasis added) – a concept that seems to require at least some outward manifestation of a manufacturer's intent that a product be put to a particular use; and at least one agency statement has acknowledged that the mere foreseeability of off-label use, standing alone, cannot be used to determine the ''intended use'' of a product. *See* Letter from Daniel Troy (FDA Chief Counsel) to Jeffrey N. Gibbs, October 17, 2002 (noting that if the FDA were to treat ''foreseeable'' off-label use as ''intended,'' it would subject off-label use to ''unintended regulation''). If manufacturer knowledge of off-label use by itself could be a basis for liability, the freedom of physicians to prescribe approved products for off-label indications would be meaningless because no manufacturer could sell any drug known to be prescribed off label.

Nevertheless, section 201.128 does state that objective intent may be determined not just by ''expressions'' but also by the ''circumstances surrounding the distribution of the article''[10]; and even if foreseeable off-label use by itself cannot establish intended use, the government might contend that such ''circumstances'' can include the distribution of the product with the knowledge that it will be used off label.

Notably, in its recent Draft Guidance, the FDA emphasized that ''intended use'' may be determined from ''any . . . relevant source'' and even cited one case for

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tion of Caronia, as an impermissible prohibition of protected speech: the court observed generally that ''the government has treated promotional speech as more than merely evidence of a drug's intended use — it has construed the FDCA to prohibit promotional speech as misbranding itself.'' 703 F.3d at 155.

[9] Erica Teichert, FDA Official Says Off-Label Ruling Won't Limit Enforcement, Law360, January 30, 2013, http://www.law360.com/articles/411478/fda-official-says-off-label-ruling-won-t-limit-enforcement.

[10] Section 201.128 also provides that ''if a manufacturer knows, or has knowledge of facts that would give him notice, that a drug introduced into interstate commerce by him is to be used for conditions, purposes, or uses other than the ones for which he offers it, he is required to provide adequate labeling for such a drug which accords with such other uses to which the article is to be put.''

the proposition that intended use can be found where there is ''no labeling or oral statements accompanying the product.'' *See* Draft Guidance at 4 (citing *Action on Smoking and Health v. Harris*, 655 F. 2d 236, 239 (D.C. Cir. 1980); *United States v. Travia*, 180 F. Supp. 2d 115, 119 (D.D.C. 2001). These cases do not by any means show that consumer use standing alone may generally be used as evidence of ''intended use.'' In fact the cases cited by the FDA indicate that an inference of ''intended use'' based solely on consumer use is proper only in very limited circumstances—where consumers use the product ''nearly exclusively'' for the ''intended use'' at issue, see *ASH*, 655 F.2d at 239-40, or where a unique context essentially precludes any inference that the product could be used for any purpose other than the ''intended use'' that the government seeks to prove, see *Travia*, 180 F. Supp. 2d at 116-19 (regarding the sale of nitrous-oxide balloons outside a rock concert). That said, the Draft Guidance does appear to reserve for the government the right to rely on known customer use for an off-label indication as evidence of manufacturer ''intended use.''

With this very broad concept of the evidence it can offer to prove intended use, and a desire to present cases as based on conduct (distribution for an unapproved intended use) rather than on off-label speech *per se*, the government may very well be inclined to place greater emphasis in its investigations on the mere distribution of drugs known to be used off label—perhaps combined with internal documents interpreted to suggest a company was motivated to make off-label sales. This kind of increased scrutiny of internal documents like strategic and business plans is highly perilous for even the most scrupulously compliant company, because there are many perfectly legitimate, and indeed compelling, reasons for manufacturers to keep track of, research, and provide information about off-label uses. Similarly, and even more obviously, the more the government comes to regard the mere sale of products known to be used off label as support for a misbranding case, the more dangerous the landscape becomes for manufacturers.

## *Conclusion*

In his address at the CBI conference, AAG Delery aptly emphasized the importance of ''transparency about the conduct'' that the government investigates and its commitment to ''clarifying the factual basis'' for its actions. Yet by focusing on the inherently difficult concept of intended use rather than promotional speech, his remarks leave room for speculation about exactly what conduct and communications the government regards as a proper factual basis for enforcement action. Ironically, by compelling the government to cast its actions as aimed at conduct and intent, and by causing it to focus on factors in addition to speech in building its cases, First Amendment concerns may have made it more difficult than ever for the government to explain, and for industry to understand, what conduct may give rise to criminal prosecutions or civil claims.

Accordingly, although the long-term prospects may look favorable for those who believe that the First Amendment protects truthful off-label communications about drugs and devices, in the short run, *Caronia* and other developments in First Amendment law may have made life more complicated for anyone advising clients on how to stay within the law as the government conceives of it.

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