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REPORT

If You Smell Smoke, When Do You Report the Fire? The Impact of the Matrixx Case on Disclosure of Adverse Event Reports

By Stephen M. Goodman

Under the recently decided case of *Matrixx Initiatives Inc. v. Siracusano*,[1] the U.S. Supreme Court held that reports of ''adverse events''[2] that were experienced by a small number of users of a Matrixx product could constitute a material fact which should be disclosed, even if the reports were not ''statistically significant'' evidence that the adverse event was caused by the product. In coming to this conclusion, the court found that other, ''contextual'' factors lent support to the reports and that therefore (as stated in *Basic Inc. v. Levinson*[3]) there was arguably ''a substantial likelihood that the disclosure of the omitted fact [i.e., the potential existence of a causal relationship] would have been viewed by the reasonable investor as having significantly altered the 'total mix' of information made available.''

While reasonably clear on its face and consistent with the court's earlier jurisprudence on materiality, the decision highlights the unusual challenges presented to biotech and pharmaceutical companies by adverse event reports. The court's reasoning in the case suggests that such companies may wish to review more frequently reports associated with their products to ensure

[1] 563 U.S. _____ (2011) (9 PLIR 359, 3/25/11).

[2] ''*Adverse event means any untoward medical occurrence associated with the use of a drug in humans, whether or not considered drug related.*'' 21 C.F.R. § 312.32 (2010).

[3] 485 U.S. 224 (1988)

Stephen M. Goodman (sgoodman@pryorcashman.com) is co-head of the Mergers and Acquisitions Practice at Pryor Cashman LLP.

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that their public statements regarding those products reflect risks that may be material as soon as possible.

Matrixx, which makes the cold remedy Zicam, had been presented with reports claiming that a small number of patients using nasally administered Zicam had lost their sense of smell, a condition known as ''anosmia.'' At the time, there was no formal study demonstrating that zinc glucomate, the active ingredient in Zicam, was the direct cause of the anosmia, although there were studies linking the use of zinc sulfate, a related compound, to loss of the sense of smell. Matrixx's vice president for research and development had apparently been unaware of these studies but was advised of them by an outside researcher in September, 2002.

It is clear that Rule 10b-5[4] does not require a publicly traded pharmaceutical company to respond to completely unsubstantiated rumors of adverse drug events.[5] What is more, an issuer's decision to respond to speculative information may itself create problems for the company. Publicizing a rumor of a drug's adverse effect, even to rebut it, may endanger confidence in the drug and thus its commercial value, potentially depressing the company's share price.

Thus, when a drug company such as Matrixx receives isolated complaints of adverse events, the natural reaction is to discount any inference of causality as speculative and therefore to treat the reports like rumors. In such a situation, the company might readily conclude that the reports are not material, and therefore that it has no obligation to disclose them.

In fact, during oral argument, the lawyers representing Matrixx sought to stress exactly this—namely, that the adverse event reports were not ''proof'' of causation. They argued that if a ''psychic'' or a ''lunatic'' had claimed there was a problem with the drug, ''that's not the kind of information a reasonable investor would rely on.''

The Supreme Court acknowledged that adverse event reports do not ''prove'' causality. It pointed out that an ''adverse drug experience'' is defined by the Food and Drug Administration as ''[a]ny adverse event *associated* with the use of a drug in humans, *whether or not considered drug related*.''[6] The FDA itself describes the limitations of such reports as follows:

> First, there is no certainty that the reported event was actually due to the product. *FDA does not require that a causal relationship between a product and event be proven, and reports do not always contain enough detail to properly evaluate an event.* Further, FDA does not receive all adverse event reports that occur with a product. Many factors can influence whether or not an event will be reported, such as the time a product has been marketed and publicity about an event. Therefore, [the Adverse Event Reporting System] cannot be used to calculate the incidence of an adverse event in the U.S. population.[7]

Furthermore, in its *Matrixx* opinion, the Supreme Court affirmed that ''[a]pplication of *Basic's* 'total mix' standard does not mean that pharmaceutical manufacturers must disclose all reports of adverse events. . . . The fact that a user of a drug has suffered an adverse event, standing alone, does not mean that the drug caused the event.''

Thus, at first blush, Matrixx's position that there was no ''proof'' of any causal relationship between Zicam use and anosmia seems reasonable. It defended its actions by claiming that the ''adverse event reports'' of anosmia did not demonstrate a ''statistically significant correlation'' between the use of Zicam and anosmia—that they only showed that ''the user of a drug experienced an adverse event at some point during or following the use of that drug.''[8] Because the causal relationship was questionable, Matrixx took the view that not disclosing the adverse event reports could not be considered material.

The Supreme Court, however, disagreed. According to the court, ''this is not a case about a handful of anecdotal reports, as Matrixx suggests.'' Rather, according to the opinion, the ''source, content and context'' of the reports should be evaluated. The court stated, ''This contextual inquiry may reveal in some cases that reasonable investors would have viewed reports of adverse events as material even though the reports did not provide statistically significant evidence of a causal link.''

In the case before it, the court identified several such ''contextual'' facts: three medical professionals and researchers had provided information about more than 10 patients who had lost their sense of smell; four product liability lawsuits had been commenced; and that a presentation regarding a possible causal link between zinc glucomate and anosmia had been made by experienced clinicians to a national medical conference devoted to treatment of diseases of the nose. Finally and ''critically,'' the court pointed out that the company had been advised that studies of a related compound, zinc sulfate, had in fact demonstrated a causal link between ''intranasal application of zinc and anosmia.'' Matrixx became aware of those studies in late 2002, but as of the class period from late 2003 to early 2004, Matrixx still had not conducted any research of its own relating to anosmia.

In the court's view, the cumulative effect of these additional facts meant that the adverse event reports and the scientific findings could not simply be dismissed by the company on the basis that they were not ''statistically significant.'' It found that the information provided to Matrixx should have been considered sufficient to establish a plausible causal connection which would have been of interest to investors. It therefore held that,

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[4] 17 C.F.R. 240 10b-5.

[5] ''A company has no duty to correct or verify rumors in the marketplace unless those rumors can be attributed to the company.'' State Teachers Retirement Bd. v. Fluor Corp., 654 F.2d 843, 850 (2d Cir. 1981); *accord* Elec. Specialty Co. v. Int'l Controls Corp., 409 F.2d 937, 949 (2d Cir. 1969) (''While a company may choose to correct a misstatement in the press not attributable to it, . . . we find nothing in the securities legislation requiring it to do so.'')

[6] 563 U.S. ____, at ___ , fn 5, citing 21 CFR § 314.80(a) (2010). (Emphasis added.) As noted in the court's footnote, adverse event reports were not required to be filed by Matrixx during the period in question, although Congress enacted legislation in 2006 obligating manufacturers of over-the-counter drugs to file such reports. See also footnote 2 above.

[7] Adverse Event Reporting System (AERS), http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/default.htm (viewed April 4, 2011) (Emphasis added.)

[8] As late as Feb. 29, 2004, Matrixx filed a Form 8-K reporting that a scientific panel it had convened to review the issue was of the opinion that there was ''insufficient scientific evidence'' to establish a direct link between the use of zinc glucomate and the loss of a sense of smell.

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assuming the plaintiffs' allegations were true for purposes of ruling on Matrixx's motion to dismiss, the plaintiffs had properly pleaded the ''materiality'' element required to sustain an action under Rule 10b-5.

A careful review of the court's cited factors confirms that without the zinc sulfate studies the court might not have resolved the issue in favor of requiring disclosure. The adverse event reports themselves only indicated incidence of anosmia in a very small number of patients, relative to the total universe of those taking the drug. As Matrixx asserted and the court agreed, such reports are not themselves probative of causality. Further, use of such reports as the basis for product liability suits does not increase their probative value. Even the scientific presentation at the national medical conference only represented informed speculation by the doctors involved, since they had not done further studies.

This leaves only the results of the zinc sulfate studies as the key fact in the ''total mix.'' The decision seems to imply that once Matrixx became aware of the existence of these studies, it needed to address the implications of the other facts more seriously. The court appeared uncomfortable with the fact that, despite its knowledge of these studies, Matrixx had undertaken no independent research to distinguish the effects of zinc glucomate from zinc sulfate. Nevertheless, it continued in its public statements to aggressively deny that there was any link between Zicam and anosmia. [9]

The court's discomfort with Matrixx's lack of research and aggressive denials may also have been compounded by the fact that in January 2004 the FDA had initiated an investigation based on the information then available. The decision seems to indicate that if the referenced facts caused drug safety regulators to become concerned with the possibility of a causal link, those facts also should have caused the drugmaker to adjust its behavior in some fashion. The court quoted from the FDA's report, *The Clinical Impact of Adverse Event Reporting*: ''[A]chieving certain proof of causality through postmarketing surveillance is unusual. *Attaining a prominent degree of suspicion is much more likely, and may be considered a sufficient basis for regulatory decisions*.''[10]

The implication is that, if management determines there is a ''prominent degree of suspicion'' of causality, then there is a ''sufficient basis'' to require further investigation of the facts and therefore appropriate modification of the issuer's public statements regarding the adverse event reports. As a result, regular review of adverse event reports regarding any significant product is strongly recommended. Management also should assess on a regular basis whether anything has occurred that may arouse ''a prominent degree of suspicion'' regarding the causal relationship between the drug and the reported event. If there has been such an occurrence, the issuer needs to confront the possibility that the ''total mix'' standard for materiality has been satisfied, in which case management should develop a strategy for addressing the ''suspicion,'' and decide what, if anything, it wants to disclose. At a minimum, an internal review of all adverse information regarding the product should be conducted prior to any presentations, earnings calls or other contacts with the investing public to ensure appropriate and consistent treatment of the suspicion.

Additionally, the company may want to take more general ''prophylactic'' measures. Adverse event reports are available by Freedom of Information Act request. Obtaining such reports on an ongoing basis and evaluating their possible impact should be made part of internal reporting. Stronger risk disclosures in public filings, specific to each material product or proposed product, may be desirable. While such disclosures may not insulate the company entirely from liability for failure to disclose a particular adverse fact, if investors are warned about the potential vulnerabilities of significant products, realization of one of these risks may have a somewhat more muted impact on the market.

Despite reaffirming the standard approach to materiality analysis, the court's decision in *Matrixx* does not offer much guidance as to when a ''suspicion'' of causality becomes a ''prominent suspicion.'' It is hard to escape the impression that the case makes it riskier not to disclose the possibility of a causal relationship when the first suspicion of causality arises. If an issuer does not make such early disclosure, it risks claims of 10b-5 liability as soon as additional information emerges which seems to support the existence of such a relationship. In other words, as a result of *Matrixx*, the first whiff of smoke may force a drugmaker to make a public disclosure of the possibility that its drug is causing a fire, even though it may ultimately be shown that the smoke came from some unrelated source.

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[9] Despite the information communicated to it in September 2002 regarding the zinc sulfate studies, Matrixx management continued to make positive statements about the company's revenue prospects, of which Zicam was a major factor. In November 2003, management modified its disclosures for the first time to indicate that ''possible'' product liability suits could have a material adverse effect on the company ''whether or not proven to be valid.'' However, they did not disclose that two such suits already had been brought.

Furthermore, as noted in the text, the product liability suits caused FDA to announce it was ''looking into'' a possible link in January 2004. News of this investigation caused a significant decline in the company's stock. On Feb. 2, 2004, the company issued a press release which attacked intimations of a causal link as ''unfounded and misleading'' and claimed that the clinical studies which had been done had not resulted in a ''single report'' of loss of smell.

After this release, the company's stock price recovered. Then on Feb. 6, the television news show *Good Morning America* ran a story describing the presentation at the professional society and the product liability suits, again causing the stock to decline substantially. Matrixx's response was to reissue the content of its earlier Feb. 2 statement. And, as noted in footnote 8, on Feb. 29, 2004, Matrixx filed a Form 8-K, reporting that a scientific panel it had convened to review the issue was of the opinion that there was ''insufficient scientific evidence'' to establish a direct link between the use of zinc glucomate and the loss of a sense of smell.

[10] The Clinical Impact of Adverse Event Reporting, page 7, http://www.fda.gov/downloads/Safety/MedWatch/UCM168505.pdf. (Emphasis added.)