



# FDA Regulatory and Compliance Monthly Recap



## MARCH 2015

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### FDA issues guidance on meetings between agency and sponsors to promote consistency and effectiveness

*The agency is making recommendations on formal meetings about the development and review of drugs or biological products that fall under the regulation of the Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER) in a bid to provide consistent procedures promoting well-managed and effective meetings.*

Every year, the FDA takes part in meetings requested by companies seeking advice about developing and reviewing investigational new drugs (INDs) and biologics or drug and biological product marketing applications. The meetings can be categorized into three types – A, B or C. The good meetings management practices (GMMPs) included in the guidance document are meant to provide consistent procedures that promote well-managed meetings and ensure that these are scheduled within a reasonable time, conducted efficiently and documented appropriately.

The [guidance](#) goes over the principles of GMMPs and explains standardized procedures for requesting, preparing, scheduling, conducting and documenting meetings. It was updated in accordance with the [Prescription Drug User Fee Act \(PDUFA\) Reauthorization Performance Goals and Procedures FY 2013 through 2017](#), and revises the 2009-issued Formal Meetings Between the FDA and Sponsors or Applicants. Among noteworthy amendments were the addition of a written response meeting format for pre-IND applications and Type C meetings, the addition of a meeting package in Type A meeting requests, and the designation as a Type B meeting about risk evaluation and mitigation strategies or post-marketing requirements occurring beyond the context of the review of a marketing application, among others.

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Specifically, the document lays out the FDA's expectations regarding meeting requests, including how they should be submitted and what information should be included, and goes over its process for evaluating requests, including what happens when a meeting is denied or granted. Requesters are advised to include 13 pieces of information when requesting a meeting, including its purpose and objective, a proposed agenda and list of questions, and the meeting type – even though the CBER or the CDER will ultimately determine this. Companies requesting type A meetings can expect a response within 14 days of receipt, while those requesting types B and C meetings will receive a response within 21 days.

Examples of circumstances under which companies should reschedule or cancel are also provided. The FDA recommends that companies reschedule when the submission of a meeting package is delayed or a critical attendee can no longer attend at the scheduled time, and cancel when the package isn't received in the specified time frame or it's totally inadequate.

The document also provides guidance on meeting packages, including the timing of submissions per meeting type, and where and how many copies should be sent. The FDA lists 11 key pieces of information that the meeting package should contain, and advises companies to organize the package in accordance with the proposed agenda. The guidance advises companies to include summary information about the product as well as the results of relevant studies and trials, specifying that the description of a result as "significant" is inadequate. The document also notes that the whole package content must support the meeting's objective, and finishes by covering pre-meetings and communications, meeting conduct and documentation, and resolution of disputes regarding meeting minutes.

## **FDA approves Novartis' Zarxio as the first biosimilar in the U.S., clearing the drug for the same indications as Neupogen and giving it a placeholder nonproprietary name**

*The regulator granted a landmark approval to the copycat version of the already approved drug in the U.S., opening up the market to less expensive copies of biological products, while uncertainty related to a naming policy remains.*

The FDA [granted](#) approval to Novartis unit Sandoz's Zarxio for the same indications as its biosimilar, Amgen's Neupogen.

The biosimilar product was approved under the Biologics Price Competition and Innovation Act of 2009, which was passed as part of the Affordable Care Act, and which created a pathway for biological products shown to be "biosimilar" to or "interchangeable" with an FDA-licensed biological product. The pathway allows the FDA to rely on existing scientific knowledge concerning the safety and effectiveness of an FDA-approved biological product – or reference product – and to clear a biosimilar biological product based on less than a full complement of product-specific preclinical and clinical data. Therefore, in order for a biosimilar product – which is generally derived from a living organism – to be granted approval, it must be demonstrated that it's "highly similar" to a biological product that's already approved, and that its safety and effectiveness are similar to those of the reference product.

Zarxio's approval was based on the FDA's review of evidence that included structural and functional characterization, animal study data, human pharmacokinetic and pharmacodynamics data, clinical immunogenicity data, and other clinical safety and effectiveness data – which showed Zarxio as biosimilar to Neupogen.

While the FDA cleared Zarxio as biosimilar, it did not approve it as interchangeable, meaning that a

pharmacist can't substitute it for the reference product without a health care practitioner being involved in the decision.

It's worth noting that the FDA's naming policy for biosimilar and other biological products remains uncertain. Since draft guidance hasn't yet been issued, the FDA designated a placeholder nonproprietary name for Zarxio – “filgrastim-sndz” – specifying that the move doesn't reflect its thinking on the issue.

As reported by the [Wall Street Journal](#), “Biosimilars have been on sale in Europe since 2006, where their use has grown slowly, according to Michael Kleinrock, research director at the IMS Institute for Healthcare Informatics. Biosimilars have grabbed more than a 50 percent market share in the U.K. and Germany, and less than 40 percent in France.”

Kleinrock anticipates that biosimilar use in the U.S. will build at a similar pace, with the drugs eventually accounting for as much as 70 percent of prescriptions.

### **OPDP warning letter states that Discovery Laboratories' website for Surfaxin makes unsubstantiated superiority claims, lacks adequate directions for unapproved use**

*Discovery Laboratories was warned by the regulator after a review of its website revealed that the company made unsupported superiority claims about Surfaxin as well as claims indicating that the RDS-prevention drug is intended for a use for which it lacks approval and for which its labeling fails to bear adequate direction.*

The [letter](#) states that the [home page](#) of the company's website for Surfaxin is false or misleading because it makes superiority claims that weren't proven by substantial evidence or clinical experience. Consequently, the webpage misbrands the product, approved for the prevention of respiratory distress syndrome (RDS), and renders its distribution “violative,” the OPDA wrote.

According to the letter, the claims “Surfaxin, the only available synthetic alternative to animal-derived surfactants approved by the FDA” and “Join the Therapeutic Evolution ... ,” which are presented alongside graphics of a pig, a cow and a humanlike robot, misleadingly imply that the drug is superior to animal-derived surfactants like Curosurf and Survanta. The FDA wrote that there doesn't appear to be any substantial evidence to support Surfaxin's claim of superiority to these, nor are there any references cited to back up the claims. The letter also cites a lack of evidence or cited references to back up a number of other claims, including that one of Surfaxin's ingredients works as a “mimic” of endogenous human SP-B.

The letter also targets the claim “Direct clinical comparisons to Exosurf, Exosurf and Curosurf,” which the webpage supports by citing two publications describing clinical studies used for Surfaxin's approval. The OPDP wrote that the studies don't constitute substantial evidence to support a direct clinical comparison claim because they either measured the efficacy of the drug only in comparison to another synthetic surfactant or only supported the safety of the drug. Another study cited by Discovery to support superiority claims was also targeted by the agency, which said that because the survey described in the study didn't include measures specifically assessing Surfaxin against its comparators, the results can't support any superiority claim.

The FDA also took issue with the company's use of the phrase “therapeutic evolution” because it is implying that Surfaxin may be safer than animal-derived surfactants, but the “Adverse Reactions” section of the PI indicates that it isn't.

The letter also states that other claims on the company's website for Surfaxin, including that it's the “only available alternative to animal-derived surfactants approved by the FDA,” are misleading because the drug is exclusively approved for the prevention of the syndrome in high-risk infants – while

Curosurf, for example, is indicated for the treatment of RDS. Thus Surfaxin is not an alternative to animal-derived surfactants. According to the letter, the PI for Surfaxin doesn't indicate that the drug can be used to treat RDS, and sufficient information demonstrating that it's safe and effective for this intended use wasn't submitted to the FDA. Therefore, Surfaxin has an intended use for which it lacks approval, and its labeling fails to provide adequate direction use.

### **FDA warns NanoBiotech Pharma for using metatags and social media to make improper claims about its products**

*The regulator sent a warning letter to the life science company for using metatags to supplement the improper promotion of its products as drugs, as well as making unapproved claims on Facebook, LinkedIn and its website.*

[NanoBiotech Pharma](#) was [warned](#) by the FDA for making therapeutic claims about its NanobacTX, a "non-prescription oral nanobiotic compound," and Urobac, "a nanobiotic compound," that render them drugs. According to the letter, because the company references uses for the products that aren't recognized as safe and effective, including that they treat, cure, mitigate or prevent disease, NanobacTX and Urobac are both unapproved new drugs and misbranded drugs.

In addition to targeting claims made on NanoBiotech's website, including the presence of testimonials recommending or describing use of the products in the treatment of disease and the citation of articles on their use to treat disease, the FDA reprimands the company for using metatags, Facebook and LinkedIn to make or supplement unapproved claims.

As reported by [RAPS](#), the FDA's first reported warning to a company over its use of metatags was in 2008, and the agency has since sent around five other letters taking issue with companies' use of metatags in their advertising.

The FDA's letter to NanoBiotech states that the company's referenced citations and other claims were "supplemented by metatags," which were used to bring Web users to its websites via Internet searches. The company used metatags including "CAC," "CAD," "coronary artery disease," "has heart disease been cured," "Heart Disease," "Calcification," "chronic prostatitis," "kidney stones," "glaucoma," "amd" (age-related macular degeneration), "bph" (benign prostatic hyperplasia), "IC," "interstitial cystitis," "cataracts" and "ED" (erectile dysfunction).

NanoBiotech was also warned about improper claims for NanobacTX and Urobac made on its Facebook and LinkedIn pages, where the products can be directly bought. The claims include that NanobacTX can reverse atherosclerosis and the underlying pathologies, and that Urobac can be used for kidney stones, PKD, chronic prostatitis and BPH, among other things.

### **OPDP sends warning letter to UCLA for promoting investigational new drug on TauMark website**

*The regulator warned UCLA, a partner in TauMark and the sponsor of the investigational new drug FDDNP, that it is violating the FD&C Act by promoting the brain diagnostic drug without market authorization and by failing to include adequate directions for use.*

UCLA, which is the sponsor of FDDNP, received a warning [letter](#) from the FDA after the regulator found that the [website](#) for its investigational new drug implies that the product is safe or effective for the purpose for which it is being investigated. According to the letter, FDDNP is consequently misbranded.

The OPDP took issue with the website's description of FDDNP for use in brain PET scans to diagnose traumatic brain injuries, Alzheimer's disease and other neurological conditions, stating that the uses require a prescription and supervision of a medical practitioner. Therefore, adequate direction for lay use can't be written, rendering the drug misbranded. The

letter further notes that UCLA's investigational drug fails to satisfy the requirements for an exemption from adequate directions for use by promoting the product and representing that it's safe and effective for the purpose it is being investigated for.

The letter also targets a number of claims and presentations on the website, including that TauMark is intended for "prevention and intervention," is an "easy and safe method," and stating that they imply "in a promotional context" that FDDNP is safe and effective for such uses even though the FDA hasn't granted approval for any use.

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For more information on any of these FDA regulatory and compliance updates, please contact [Scott S. Liebman](mailto:sliebman@loeb.com) at [sliebman@loeb.com](mailto:sliebman@loeb.com).

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