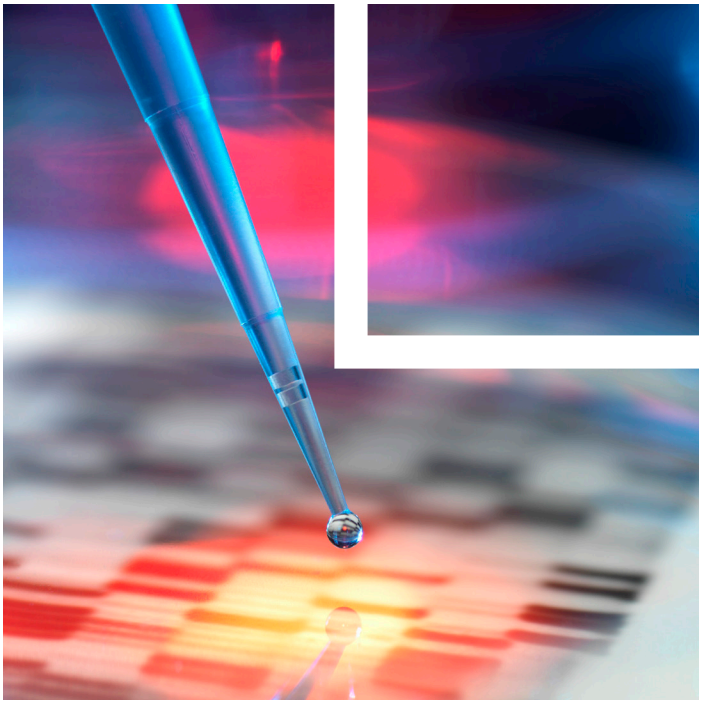
FDA Regulatory & Compliance Monthly Recap
July 2020



FDA issues guidance on providing electronic regulatory submissions for medical devices

The guidance clarifies the agency's interpretation of the statutory requirements for electronic submissions, including which submissions must be submitted solely in electronic format. The document also outlines which submissions are exempt from electronic format requirements as well as the process used by the FDA to specify the electronic formats for submissions.

The FDA published a guidance that provides clarification on the requirements for electronic submissions under the Federal Food, Drug, and Cosmetic Act (FDCA). The guidance describes the submission types that must be submitted electronically, the timetable and process for implementing those requirements, and the criteria for waivers and exemptions from those requirements. In addition, the document outlines the process the agency will use to issue specific guidances relating to specific submission types. The agency hopes that this clarification will provide consistency as well as streamline the process for implementing electronic submissions under the FDCA. Submissions not prepared in the proper format will not be filed or received unless they have been given an exemption. Under the guidance, submissions solely in electronic format will be required for the following types of submissions:

- Premarket notification submissions (510(k)s) under Section 510(k)
- Evaluation of automatic class III designation requests (de novos) under Section 513(f)(2)
- Premarket approval applications (PMAs), including Transitional PMAs under Sections 515(c), 515(d)
- Modular PMAs under Section 515(c)(4)
- Product development protocols under Section 515(f)
- Investigational device exemption applications under Section 520(g)
- Humanitarian device exemptions under Section 520(m)
- Emergency use authorizations under Section 564
- Certain investigational new drug applications under Section 351 of the Public Health Service (PHS) Act
- Certain biologics license applications under Section 351 of the PHS Act
- Pre-submissions

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The guidance also highlights criteria for exemptions from the submission solely in electronic format requirements, which includes expanded access to compassionate use requests as well as emergency use reports and adverse event reports. However, in order to facilitate the review process, the FDA still encourages electronic submission of the aforementioned submission types as templates become available. Any additional exemptions, when applicable, will be outlined in individual guidances for each type of submission. Furthermore, the agency may recommend electronic submission formats for Master Access Files, 513(g) Requests for Information and Clinical Laboratory Improvement Amendments.

The agency will develop guidance documents to specify the electronic formats, subject matter and scope of applicability for submissions, with plans to release these documents on the FDA's website sequentially, allowing for a phased implementation. A notice will then be published in the Federal Register and identify a comment period for the draft guidance. Once review of the draft guidance is completed, the agency will post a notice in the Federal Register that the final guidance is available on the FDA website. Further revisions or updates to the formats will be announced on the website and published in the Federal Register.

FDA issues four guidances to assist sponsors with new animal drug applications

The FDA's Center for Veterinary Medicine (CVM) issued four draft guidances providing recommendations to sponsors preparing data submissions for new animal drug products. The guidances were designed to help animal drug manufacturers incorporate alternative approaches into their proposed clinical investigation protocols. These recommendations are aligned with those already issued by the FDA's other medical product centers.

The FDA's CVM issued four draft guidances to help sponsors prepare data submissions for new animal drug products. The first guidance, "Use of Data from Foreign Investigational Studies to Support Effectiveness of New Animal Drugs," outlines principles for designing, conducting and reporting results from foreign studies in submissions to the CVM regarding study protocols for new drugs. The guidance highlights the types of foreign studies that would be considered for acceptance, including studies demonstrating substantial evidence of effectiveness, adequacy of foreign data for regulatory use, field effectiveness studies, laboratory effectiveness studies, foreign data applicable to the U.S. population and foreign bioresearch monitoring. The guidance also outlines the criteria needed for a foreign study to be successfully submitted. Finally, the guidance examines requirements for translations of foreign languages as well as for converting units of measurement to be consistent with the imperial system.

The second guidance, "Use of Real-World Data and Real-World Evidence to Support Effectiveness of New Animal Drugs," provides recommendations on how sponsors can incorporate real-world data (RWD) and real-world evidence (RWE) into proposed clinical investigation protocols and applications for new animal drugs. The guidance provides definitions for both RWD and RWE and outlines how they each can be applied to new animal drug investigations, as well as how the CVM will evaluate both. This includes study design recommendations, determinations of suitability for regulatory use, potential sources, and general considerations regarding both RWD and RWE.

In the third guidance, "Biomarkers and Surrogate Endpoints in Clinical Studies to Support Effectiveness of New Animal Drugs," the CVM provides clarification on how it intends to evaluate biomarkers, including surrogate endpoints, on whether they can be used to support substantial evidence of effectiveness for a new animal drug application (NADA) or a reasonable expectation of effectiveness for a conditional NADA (CNADA). The guidance examines the use of biomarkers in effectiveness studies and highlights different categories of biomarkers, as well as their use in different stages of drug development. In addition, the guidance outlines labeling considerations when biomarkers and surrogate endpoints are used as primary variables to demonstrate effectiveness.

The final guidance, "Adaptive and Other Innovative Designs for Effectiveness Studies of New Animal Drugs," offers recommendations to sponsors that may benefit from the use of adaptive and other innovative designs to demonstrate substantial evidence of effectiveness

or a reasonable expectation of effectiveness in NADAs and CNADAs, respectively. The guidance outlines the differences between adaptive designs, group sequential designs, sample size re-estimation and other design adaptations, as well as their advantages and disadvantages. It also discusses recommendations for combining several types of adaptive features.

All four guidances also outline the process for sponsors to receive feedback from the CVM in regard to the incorporation of any of the aforementioned topics in the development of new animal drugs.

FDA updates guidance on conduct of clinical trials during the COVID-19 pandemic to address methods of obtaining electronic informed consent

The FDA updated the Q&A appendix in its guidance on conducting clinical trials during the COVID-19 pandemic. The updates discuss suggested methods for researchers to obtain informed consent from hospitalized patients in isolation. The update also outlines the process for obtaining such consent as well as clarifies recommendations on documenting details when utilizing videoconferencing for trial visits.

The FDA updated guidance providing clarification for two previously suggested methods of obtaining informed consent from a hospitalized patient in isolation. While the agency urges researchers to use traditional methods whenever possible, the guidance outlines specific procedures to obtain informed consent if traditional methods are unavailable. The methods and procedures discussed are:

Method 1: A photograph of the signed informed consent document can be sent to trial staff.

1. An unsigned copy of the document is provided by an individual who has access to the patient.
2. The researcher arranges a telephone or videoconference call to review the document with the patient and answer any questions regarding the treatment.
3. The patient, or another individual in the room, photographs the signed document and transmits it to the researcher.
4. The trial team enters the photograph into trial records, along with an attestation stating that the photograph is of the informed consent document signed by the patient and how it was obtained.

Method 2: A witness can attest to the signature, but a photograph of the signed informed consent document cannot be sent to trial staff.

1. An unsigned copy of the document is provided by an individual who has access to the patient.
2. The researcher arranges a telephone or videoconference call and a witness who is not connected in any way to the investigation reviews the document and answers any questions regarding the treatment. Instead of a witness, a recording of the conversation can be made.
3. When using this method, documentation in trial records must include a signed and dated attestation by the witness who participated on the call that the patient confirmed their agreement to participate in the trial and signed the document. In addition, a signed and dated attestation by the researcher stating why the signed document was not obtained must be included.
4. When using a recording instead of a witness, documentation must include the recording of the review call and a signed and dated attestation by the researcher stating why the signed document could not be obtained.

In addition, the guidance also outlines recommendations for best practices for researchers who need to conduct trial participant visits remotely. These include suggestions that the researcher conducting the visits should be trained on the use of real-time videoconferencing and telemedicine. Furthermore, the FDA recommends that trial teams should have processes in place to ensure the privacy of participants. The identities of both the researcher and the trial participant should also be confirmed before commencing with the visit.

FDA pilot program to test communicating patient-reported outcomes publicly

In an effort to create a consistent source of public information from cancer trials, the FDA's Oncology Center of Excellence launched Project Patient Voice*. The pilot project was developed to provide the public with access to information describing patient-reported symptoms from cancer trials for marketed treatments. The data, which is normally analyzed by the FDA during the drug approval process, is rarely included in product labeling and, as a result, is mostly inaccessible by the public at large.*

Patient-reported outcome (PRO) data provides the FDA with important disease- or treatment-related symptom information, such as the severity and/or frequency of a reported symptom or side effect. This information can provide additional information for patients to discuss with their health care professional apart from the clinician-reported safety data contained in product labeling. Project Patient Voice obtains its data directly from patients and can inform potential users of a drug about symptoms prior to, as well as throughout, treatment.

The project's website will include a list of cancer clinical trials that have PRO data available. Each trial will include a table of patient-reported symptoms, which can be selected individually to display in a bar or pie chart format to outline that symptom before treatment starts and over the first six months of treatment. This allows patients to gain valuable insights into potential side effects during each stage of treatment not currently available in standard FDA safety tables. The visuals and data included on the site are provided voluntarily by the drug companies conducting the trials.

The FDA plans a phased release of the website, the first of which will include just one trial, while the agency gathers public feedback on the manner in which the data is presented. This feedback will be used to facilitate improvements to the website in order to make the information presented in the most user-friendly way possible. AstraZeneca is the first company to provide PRO data for one of its approved cancer drugs and has worked closely with the FDA to develop the best methods to present the information in an informative way.

The agency stresses that Project Patient Voice is not meant to replace clinician-reported safety data included in drug labeling but, rather, to augment it. The FDA also recommends that the data presented on the website should not be used as a substitute for advice from a health care professional nor as a sole source of information when making decisions regarding medical treatment.

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