



Summer 2020

Brought to you by the Office of Translational Sciences (OTS) in collaboration with the Office of Communications (OCOMM) within the Center for Drug Evaluation and Research (CDER)

What's New in Regulatory Science is a quarterly newsletter from the Food and Drug Administration's (FDA's) Center for Drug Evaluation and Research (CDER). It features new developments, opportunities, and initiatives in regulatory science, with the goal of advancing medical product development.

Please share this message and the [sign-up link](#) with colleagues. If you have comments or questions, please contact us at OTSCcommunications@fda.hhs.gov.



COVID-19 UPDATES

The FDA is engaged in numerous activities to protect and promote public health during the coronavirus disease 2019 (COVID-19) pandemic. For CDER, these efforts include accelerating development of treatments for COVID-19, maintaining and securing drug supply chains, providing guidance to stakeholders, advising developers on how to handle clinical trial issues, and keeping the public informed. Information on some of CDER's efforts related directly to drugs and COVID-19 can be found in the links below:

- Coronavirus (COVID-19) Drugs Web Page
<https://www.fda.gov/drugs/emergency-preparedness-drugs/coronavirus-covid-19-drugs>
- FDA Coronavirus Treatment Acceleration Program (CTAP):
<https://www.fda.gov/drugs/coronavirus-covid-19-drugs/coronavirus-treatment-acceleration-program-ctap>

- **FDA COVID-19 Initiatives**

- FDA COVID-19 Response At-A-Glance Summary as of August 14, 2020
<https://www.fda.gov/media/137005/download>
- Innovation to respond to COVID-19
<https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/innovation-respond-covid-19>
- FDA Guidance on Conduct of Clinical Trials of Medical Products during COVID-19 Public Health Emergency
Issued on 18 March 2020 and updated most recently on 2 July 2020, this guidance emphasizes safety of trial participants as the paramount consideration during the pandemic. It also includes recommendations on protecting trial integrity and helping to maintain compliance with Good Clinical Practice and an appendix of questions and answers that is expanded with each update of the Guidance based on issues raised by stakeholders.
- Information on Conduct of Clinical Trials during the COVID 19 Pandemic
A new FDA mailbox was established at Clinicaltrialconduct-COVID19@fda.hhs.gov dedicated to COVID-19-related inquiries. As of 7 Aug 2020, 485 inquiries had been received and responses had been provided for 481 of these. Inquiries to this mailbox have informed the FDA Guidance on *Conduct of Clinical Trials of Medical Products during COVID-19 Public Health Emergency*, as mentioned above. Additional information on clinical trial conduct during the COVID 19 pandemic can be found [here](#). For information on drug development inquiries for drugs to address COVID 19, click [here](#).
- FDA-CDER COVID-19 Critical Care Drug Monitoring Survey Portal
FDA is tasked with helping to ensure that an adequate drug supply is available to meet public health needs, such as in a pandemic response. The Agency has established a voluntary self-reporting platform for hospitals and healthcare systems to provide real-world data (RWD) on their supply of COVID-19-related critical care drugs. FDA utilizes the survey responses, in addition to other available drug supply chain information, in a comprehensive way to support our mission during this public health emergency—by anticipating where demand may be expected to increase for certain drugs, as well as by enabling CDER to explore all possible actions and undertake a timely and responsive action on mitigating potential or actual drug shortages. Information and videos are available describing the [registration process](#) and [survey completion](#) steps involved.
- FDA Updates on hand sanitizers
FDA is warning consumers and health care providers that the agency has seen a sharp increase in hand sanitizer products that are labeled to contain ethanol but that have tested positive for methanol or 1-propanol contamination. FDA test results have also shown that

certain hand sanitizers are subpotent and have concerningly low levels of ethyl alcohol or isopropyl alcohol. FDA continues to update its do-not-use list of hand sanitizers at www.fda.gov/unsafehandsanitizers. FDA also continues to update the hand sanitizer [guidances](#), as needed, including clarification on impurity levels and testing ethanol for methanol to help ensure widespread access to alcohol-based hand sanitizers that are free of contamination.

- COVID MyStudies Application (App)

FDA is making its previously developed FDA MyStudies app available to investigators during the COVID-19 Public Health Emergency as a free platform to securely obtain patients' informed consent for eligible clinical trials when face-to-face contact is not possible or practical due to COVID-19 control measures. [Learn more](#).

- **FDA Collaborative Efforts with External Stakeholders to address the COVID-19 Pandemic**

- FDA Collaborations Promote Rigorous Analyses of Real-World Data to Inform Pandemic Response

FDA has entered into an agreement with Aetion to collaborate on advanced analytical techniques to answer urgent COVID-19 research questions about the use of diagnostics and medications during the pandemic, and risk factors for COVID-19-related complications in different patient populations. [Learn more](#).

- Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV)

Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) is a public-private partnership led by the National Institutes of Health (NIH) and coordinated by the Foundation for the National Institutes of Health (FNIH) to develop a research strategy for prioritizing and speeding development of the most promising COVID-19 vaccines and treatments.

ACTIV brings together NIH with its sibling agencies in the Department of Health and Human Services, including the Biomedical Advanced Research and Development Authority (BARDA), Centers for Disease Control and Prevention (CDC) and the U.S. Food and Drug Administration (FDA); other government agencies, including the Department of Defense (DOD) and Department of Veterans Affairs (VA); the European Medicines Agency (EMA); and representatives from academia, philanthropic organizations and biopharmaceutical companies. [Learn more](#).

- CURE ID App:
Last December, FDA in collaboration with the NIH's National Center for Advancing Translational Sciences (NCATS), launched a data-sharing app called CURE ID. The CURE ID platform is an internet-based repository that allows clinicians to report novel uses of existing drugs for difficult-to-treat infectious diseases through a website, a smartphone or other mobile device.



FDA and NIH along with the Critical Path Institute have made updates to the CURE ID crowd-sourcing app to make it easier for healthcare providers to share — via mobile device or website — their experiences treating COVID-19 patients who are unable to be enrolled in a clinical trial. CURE ID's web-based repository lets providers share experiences with novel uses of existing drugs in treating difficult-to-treat infectious diseases. Healthcare providers worldwide are encouraged to share their COVID-19 treatment experiences via CURE ID. [Learn more.](#)

- Partnering with the European Union and Global Regulators on COVID-19
The FDA and the EMA have been exchanging information on the rapidly evolving scientific landscape of products and clinical trials and, as possible, discussing the interpretation of data supporting regulatory decisions. [Learn more.](#)
- COVID-19 Educational Resources
[FDA has assembled educational videos, podcasts, social media tool kits, consumer articles, and other resources to help inform various stakeholders about the COVID-19 pandemic.](#)

COVID-19 FDA NEWS RELEASES

★FDA revokes the emergency use authorization (EUA) for chloroquine phosphate and hydroxychloroquine sulfate to treat certain hospitalized patients with COVID-19

On June 15, FDA revoked the EUA that allowed for chloroquine phosphate and hydroxychloroquine sulfate donated to the Strategic National Stockpile to be used to treat certain hospitalized patients with COVID-19 when a clinical trial was unavailable, or participation in a clinical trial was not feasible. Based on its ongoing analysis of the EUA and emerging scientific data, the FDA determined that chloroquine and hydroxychloroquine were unlikely to be effective in treating COVID-19 for the authorized uses in the EUA. Additionally, in light of observed serious cardiac adverse events and other potential serious side effects, the known and potential benefits of chloroquine and hydroxychloroquine no longer outweighed the known and potential risks for the authorized use. To learn more, go to: <https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-revokes-emergency-use-authorization-chloroquine-and>

★ **FDA Warns of Newly Discovered Potential Drug Interaction That May Reduce Effectiveness of a COVID-19 Treatment Authorized for Emergency Use**

On June 15, FDA also warned health care providers about a potential drug interaction related to the investigational antiviral drug remdesivir, which had received (EUA) for the treatment of hospitalized COVID-19 patients with severe disease. Based on a recently completed non-clinical laboratory study, the FDA revised the fact sheet for health care providers that accompanies the drug to state that co-administration of remdesivir and chloroquine phosphate or hydroxychloroquine sulfate is not recommended, as it may result in reduced antiviral activity of remdesivir. To learn more, go to: <https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-warns-newly-discovered-potential-drug-interaction-may-reduce>

 **FDA HIGHLIGHTS**

FDA ISSUES 2019 DRUG SAFETY PRIORITIES ANNUAL REPORT

The CDER Drug Safety Priorities 2019 [report](#) details CDER's work to manage drug safety issues through modernized safety surveillance methods and innovations in how CDER identifies, assesses, and addresses safety concerns. The report highlights key safety-related milestones and accomplishments of 2019, as well as the programs and initiatives at the core of CDER's drug safety operations, including the Sentinel System and the Safe Use Initiative. The report focuses on CDER's ongoing activities to help address the national opioid crisis, work in addressing unexpected impurities in medicines, and use of mobile apps and social media platforms to better understand drug safety risks.

 **CDER HIGHLIGHTS**

Research update from the Office of Biostatistics (OB)/Office of Translational Sciences (OTS) and Office of Surveillance and Epidemiology (OSE)

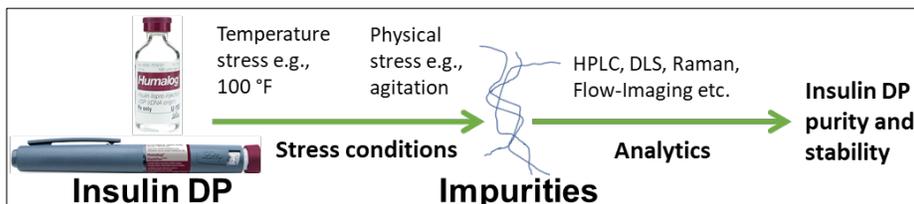
Development of the software, *geoMapr* (Geographically-enriched Machine-aided analysis of Prescription Drug Utilization Data), for enriched analysis of drug utilization data

In post-market safety surveillance, pharmacy dispensing data provide valuable insights to the Agency for the analysis of drug utilization. Our web-based software (*geoMapr*) provides tools to augment the nationally representative prescription drug dispensing data with other geographically referenced, publicly available, demographic, socioeconomic, or healthcare service data. *geoMapr* subsequently generates presentation-ready results of the surveillance data analyses, including user-interactive data tabulations, visualization, and machine learning for identifying factors highly associated with drug utilization. *geoMapr* has been used to analyze the prescribing trends for opioid antagonists such as

naloxone and buprenorphine. Future enhancement to *geoMapr* include spatial modeling to explore factors associated with geographical variations in prescription drug dispensing.

Research update from the Office of Pharmaceutical Quality (OPQ)

Identifying/Evaluating failure of insulin drug products under real world stress conditions:



Diabetic patients depend heavily on insulin drug products (DPs) to regulate their blood glucose. The Office of Biotechnology Products (OBP) in OPQ evaluates the quality of insulin DPs. OBP assessors and research labs have been working closely together as part of the OBP Insulin Working Group (IWG) to address potential quality issues related to insulin DPs. Unlike other biotechnology DPs, insulin DPs are predominantly self-administered and are available in both vial and pen presentations. OBP is looking at potential real-world storage and handling scenarios of insulin DPs by the patients beyond the standard in-use and supportive stability study conditions typically seen in a marketing application. This collaborative approach aims to improve product manufacturing, testing and surveillance to help ensure the availability of high-quality drugs, and to identify decision-making tools and resources that will enable effective risk-based decisions through best practices, analytics and research findings. The outcomes of this collaboration are to both provide internal resources for regulatory staff and publish peer reviewed manuscripts to share with the broader scientific community.

**Update from the Guidance, Policy and Communications Team, Office of Translational Sciences
Immediate Office**

FDA Publishes Guidance Snapshots: Visual Communication Tool for Clinical Trial and Drug Development
Guidance Documents



FDA launched a new pilot program in February to develop FDA guidance document snapshots. The visual guidance snapshots highlight key information from FDA guidance documents on topics that seek to modernize drug clinical trials and accelerate drug development.

FDA guidance documents represent the Agency’s current thinking on a particular topic. To support transparency and communication for FDA guidance documents, the FDA has launched the Guidance Snapshot Pilot program for a subset of cross-cutting FDA guidance documents. Guidance snapshots provide background and highlights from FDA guidance documents using visual representations and plain language. They contain supportive communications tools such as drug development timelines showing which stage to implement recommendations expressed in the guidance and guidance recap podcasts. This pilot program is intended to increase stakeholder awareness and engagement for FDA guidance documents on innovative topics.

To learn more about the FDA Guidance Snapshot Pilot Program and to view the current guidance snapshots visit the FDA Guidance Snapshot Pilot website: <https://www.fda.gov/drugs/guidances-drugs/guidance-snapshot-pilot>.

PHUSE/FDA Data Science Innovation Fridays Webinar Series

PHUSE is an expanding, global society with a global membership of clinical data scientists. Webinars are held every Friday, at 9:00 a.m. (EDT). To view the schedule, go to: [PHUSE/FDA Data Science Innovation Challenge](#)

Meet the Faces Behind FDA Science

Every day, FDA scientists carry out scientific research and regulatory actions that have a profound impact on the health and well-being of all Americans. They use their expertise to promote public health and foster therapeutic innovations. The FDA scientists highlighted in this section talk about their passion for the work they do, the Agency's pioneering regulatory science culture and opportunities for professional growth, and why they love working at FDA. Click [here](#) to read more

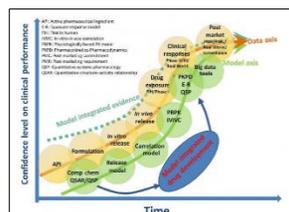
RECENT CDER IMPACT STORIES



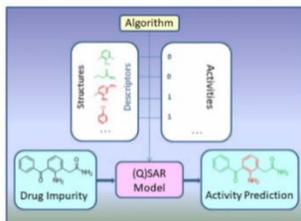
CDER is continuing to highlight its regulatory science research in a series of [regulatory science impact stories](#). Recent posts include:

CDER Statistical Studies Innovate Measures of Adhesion to Assess Generic Products Drugs delivered via transdermal patches are used to treat a wide variety of diseases and conditions, including high blood pressure, angina, hormone deficiencies, and depression. Statistical research at CDER has led to development of improved approaches for comparing the adhesion to the skin of generic transdermal drug products with that of brand name versions. These new approaches to performance testing help eliminate a major barrier to the availability of high-quality, well-adhering generic TDS products for patients. [Learn more.](#)

Modeling Tools Could Modernize Generic Drug Development The term *quantitative methods and modeling* (QMM) in the context of drug development covers a broad spectrum of tools based on computational approaches and mathematical modeling. These tools combine to form the bases of “knowledge management systems” that integrate scientific understanding and existing data about drug products. Researchers at CDER’s Office of Generic drugs have recently developed a conceptual overview of how QMM can further generic drug development. [Learn more.](#)



CDER Assessment of Drug Impurity Mutagenicity by Quantitative Structure-Activity Relationship Modeling The testing of the many low-level impurities present in some drug products for their ability to mutate DNA can be a significant burden for drug developers. CDER researchers are leading development of increasingly sophisticated and accurate computational models, including quantitative structure-activity relationship (QSAR) models, that can be used to predict the mutagenicity of these impurities. [Learn more.](#)



RECENT SPOTLIGHT ON CDER SCIENCE



CDER continues with its [Spotlight on CDER Science](#) series featuring the Center's noteworthy scientific and research-oriented activities. Recent *posts* include:

Translating In Vitro Antiviral Activity to the In Vivo Setting: A Crucial Step in Fighting COVID-19

As the international research community seeks to develop new drugs to combat COVID-19 and to assess the potential of existing drugs for this purpose, CDER researchers outline the challenges and important considerations in translating data on the in vitro antiviral activity and potency of possible drug treatments for COVID-19 to the in vivo setting, including the appropriate design of dosing regimens in clinical trials. [Learn more.](#)



IN PRESS

“Unless otherwise indicated, the opinions expressed in these articles are those of the authors and should not be interpreted as the position of the U.S. Food and Drug Administration.”

Extrapolation of adult efficacy to pediatric patients with chemotherapy-induced nausea and vomiting.

Momper JD, Heinrichs MT [...] Mulugeta Y

[J Clin Pharmacol](#) 2020 Jun;60(6):775-84

Chemotherapy-induced nausea and vomiting (CINV) is a common adverse event that impairs the quality of life of children with cancer. Momper et al. evaluated the feasibility of extrapolating efficacy results from adults to pediatric populations for drugs to treat CINV and found that extrapolation was plausible for 5-hydroxytryptamine-3 and neurokinin-1 receptor antagonist antiemetics.



The effect of drug combinations on the kinetics of the emergence of antibiotic resistance in *E. coli* CFT073 using the in vitro hollow fiber infection model.

Garimella N, Zere T [...] Weaver JL

[Int J Antimicrob Agents](#) 2020 Apr;55(4):105861

Using a hollow-fiber infection model (HFIM) to analyze the emergence of antibiotic resistance in *Escherichia coli* (*E. coli*), Garimella et al. demonstrated that double or triple antibiotic combinations significantly delayed the emergence of resistant *E. coli* subpopulations.

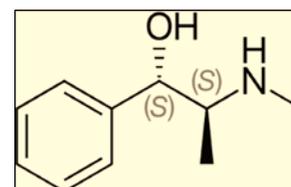


Evaluation of commercially available meth-deterrent pseudoephedrine hydrochloride products

Rahman Z, Aqueel MS [...] Ashraf M

[Int J Pharm](#) 2020 Feb 15;575:118909

As pseudoephedrine can be used as starting material for producing methamphetamine, some over-the-counter pseudoephedrine products have recently been promoting that they are “meth-deterrent.” Rahman et al. showed that pseudoephedrine is just as extractable from some products promoted as “meth-deterrent” as from products that did not make such claims.

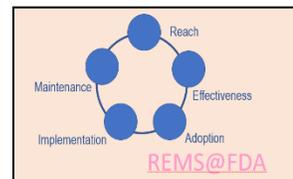


Multivariate data analysis of growth medium trends affecting antibody glycosylation.

Powers DN, Trunfio N [...] Agarabi C

[Biotechnol Prog](#) 2020 Jan;36(1):e2903

Powers et al. manufactured therapeutic antibodies in a series of microbioreactors and used multivariable analytic techniques to identify combinations of variables that were associated with desired product attributes such as specific protein glycosylations. The overall goal of the research is a manufacturing approach that will permit us to ensure critical quality attributes in the production of complex biotherapeutics.

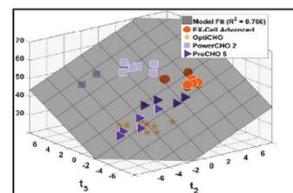


Adaptation for Regulatory Application: A Content Analysis of FDA Risk Evaluation and Mitigation Strategies Assessment Plans (2014–2018) Using RE-AIM

Toyserkani GA, Huynh L, Morrato EH

[Front. Public Health](#), 25 February 2020

The authors characterized and evaluated REMS assessment plans using the RE-AIM (Reach, Effectiveness, Adoption, Implementation, Maintenance) framework and observed heavy focus on Implementation measures. They discuss the usefulness of a systematic application of the RE-AIM framework for improving REMS programs and the potential of implementation science to benefit FDA's decision-making.



UPCOMING EVENTS

Information on upcoming meetings, conferences, and workshops sponsored or co-sponsored by CDER and be found is available on FDA webpages . For details on each event, click here.



CAREER OPPORTUNITIES



FDA continues to recruit and retain a world-class workforce dedicated to protecting and promoting the public health. Information on job vacancies, employment events, and hiring programs can be found by following [@FDAJobs](#) on Twitter and by visiting [FDA's LinkedIn page](#) and the [Jobs at CDER](#) and the [Career Opportunities at CDER webpages](#). In addition, you can contact OTS directly at CDEROTSHires@fda.hhs.gov. Help us spread the news through your social media networks!

For more information, please visit the [FDA In Brief webpage](#).

Scientific Internships and Fellowships / Trainees and Non-U.S. Citizens

Whether you're an undergraduate looking to pursue a career in science, a graduate student seeking experience in regulatory science, a postgraduate looking for fellowship opportunities, or a senior scientist pursuing research experience in your field of expertise, FDA offers you many paths to learning about the exciting field of regulatory science. Click [here](#) for more information.