Drug-Device Combination Products 101: Identifying, Developing, and Evaluating Drug-Device Combination Products

Public Training
May 10, 2023

Complex generic drug-device combination products are typically difficult to develop, which means that many of these products face less competition than non-complex products, and therefore can be more expensive and less accessible to the patients who need them. FDA and the Center for Research on Complex Generics (CRCG) are offering a training, Drug-Device Combination Products 101: Identifying, Developing, and Evaluating Drug-Device Combination Products, to support the efficient development of complex generic drug-device combination products and to discuss ways to enhance the quality of ANDA submissions for these products.

The purpose of this training is to describe FDA's regulatory expectations and practices for pre-ANDA assessment and ANDA review of generic drug-device combination products, especially those with complex device constituent parts. For these products, ANDAs should include comparative analyses between the device user interfaces of the proposed generic product and its reference listed drug (RLD) as well as data supporting the quality and performance of the overall product. As the complexity of drug-device combination products increases, challenges with product development and demonstration of substitutability may also increase.

Hybrid Experience:

The training will offer both in-person and remote attendance options for the first four sessions. The training will also include an interactive fifth session for in-person attendees only that will allow attendees to apply the learnings from the first four sessions to a mock generic drug-device combination product development process. The fifth session will offer opportunities to handle and manipulate a variety of relevant devices.

During the training, FDA, CRCG, and generic drug industry experts will share information about:

- combination product classification
- challenges with device development and comparative user interface assessment
- methods for evaluating whether differences in the user interface may increase risks for user errors compared to the RLD when generic substitution occurs, and
- demonstration of product quality and performance

FDA and the Center for Research on Complex Generics—which is a collaboration between the University of Maryland School of Pharmacy and the University of Michigan College of Pharmacy—are dedicated to advancing programs that stimulate scientific dialogue, disseminate current insights about complex generics, and generate new knowledge in support of FDA's mission to promote and protect the public health by increasing access to safe and effective generic medicines.

Learning Objectives:

- Define drug-device combination products and discuss the drug-device combination product classification process
- Discuss how human factors should inform user interface development
- Identify generic drug industry challenges and obstacles that impact various aspects of complex generic drug-device combination product development and management across the product lifecycle
- Review best practices for comparative analyses between the device user interfaces for a proposed generic combination product and its RLD
- Discuss when comparative analyses may be sufficient to justify user interface differences between a proposed generic and RLD and when additional data and/or information may be needed

- Review best practices for comparative use human factor study design, execution, and reporting and discuss FDA research on other types of studies that could provide data to support user interface differences
- Discuss GDUFA-funded research efforts to address scientific challenges and gaps that hinder development and assessment of complex generic drug-device combination products
- Discuss product quality and performance considerations for complex generic drug-device combination products such as prefilled injection pens, transdermal systems, intravaginal systems, implants, and intrauterine systems
- Discuss pre-ANDA interactions with FDA and how to leverage these opportunities to enhance ANDA submission quality for complex generic drug-device combination products

Agenda

8:30 AM – 8:40 AM	***Welcome***	
	James Polli, PhD	Co-Director, CRCG
8:40 AM – 8:55 AM	***Course Introduction***	
	Robert Lionberger, PhD	Director, ORS, OGD, FDA
Session 1:	**How to Identify Products That Are Drug-Device Combination Products: a CDER Product Jurisdiction and Office of Combination Products Perspective**	
	This session will provide an overview of the regulatory framework that defines combination products that include drug and device constituent parts. Other topics will include exploring the differences between single entity, co-packaged, and cross-labeled drug-device combination products.	
8:55 AM – 9:00 AM	***Introduction to Session 1***	
	Kimberly Witzmann, MD	Deputy Director, OSCE, OGD, FDA
9:00 AM – 9:30 AM	***Definition of a Combination Product and the Complementary and Collaborative Roles of FDA's Office of Combination Products & CDER's Product Jurisdiction Office Have on Classifying Products as Drugs, Devices, or Drug-Device Combination Products***	
	Ifeanyi U. Uwemedimo, PhD	Senior Scientific Reviewer, OCP, OCPP, OC, FDA
	Kristina Lauritsen, PhD	Combination Product Policy Advisor, PJO, OGD, FDA
9:30 AM – 9:45 AM	***Challenges in Drug-Device Combination Products – Industry Perspective***	
	Tzach Bachar, MS	Director, Regulatory Affairs, Padagis Israel Pharmaceuticals Ltd
9:45 AM – 10:15 AM	***Q&A Session with Panel***	
Moderator:	**Kimberly Witzmann, MD**	Deputy Director, OSCE, OGD, FDA
Panelists:	**Ifeanyi U. Uwemedimo, PhD**	Senior Scientific Reviewer, OCP, OCPP, OC, FDA
	Kristina Lauritsen, PhD	Combination Product Policy Advisor, PJO, OGD, FDA
	Tzach Bachar, MS	Director, Regulatory Affairs, Padagis Israel Pharmaceuticals Ltd
	Lisa Bercu, JD	Regulatory Counsel, DPD, OGDP, OGD, FDA
	John Barlow Weiner, Esq, JD	Associate Director for Policy, OC, OCPP, OCPR, FDA
	Brandon Wood, BS	Director, Regulatory Affairs, Gx Steriles, Teva Pharmaceuticals USA, Inc.
10:15 AM – 10:30 AM	***Coffee Break***	
Session 2:	**Drug-Device Combination Products and Comparative Analyses: Best Practices Prior to and for ANDA Submission**	
	This session will discuss the iterative role of human factors and risk assessment in device development or selection, and the use of comparative analyses to evaluate user interface differences between a proposed generic combination product and its RLD.	
10:30 AM – 10:35 AM	***Introduction to Session 2***	
	Kathryn Hartka, PharmD, PhD	Pharmacologist, Device Evaluation Team, DTP-I, ORS, OGD, FDA
10:35 AM – 10:50 AM	***Pre-ANDA Program Support of Generic Drug-Device Combination Product Development***	
	Kathryn Hartka, PharmD, PhD	Pharmacologist, Device Evaluation Team, DTP-I, ORS, OGD, FDA
10:50 AM – 11:05 AM	***Best Practices for ANDA Submission of Comparative Analyses for Drug-Device Combination Products & the ANDA User Interface Assessment Process***	
	Mary Lee, MD	Senior Physician, DCR, OSCE, OGD, FDA

11:05 AM – 11:20 AM	***Challenges and Learnings with Device Development and Comparative User Interface Assessment for DDCP***	
	Satyashodhan Patil, BE, PGDIBO	Deputy General Manager (R&D), Device Development, Sun Pharmaceutical Industries Limited
11:20 AM – 12:00 PM	***Q&A Session with Panel***	
Moderator:	**Kathryn Hartka, PharmD, PhD**	Pharmacologist, Device Evaluation Team, DTP-I, ORS, OGD, FDA
Panelists:	**Mary Lee, MD**	Senior Physician, DCR, OSCE, OGD, FDA
	Satyashodhan Patil, BE, PGDIBO	Deputy General Manager (R&D), Device Development, Sun Pharmaceutical Industries Limited
	Katharine B. Feibus, MD	Team Leader, Device Evaluation Team (Team D), DTP-I, ORS, OGD, FDA
	CDR Andrew Fine, PharmD, BCPS	Senior Advisor, DCR, OGD, OSCE, FDA
	Markham Luke, MD, PhD, FAAD	Director, DTP-I, ORS, OGD, FDA
	Kimberly Witzmann, MD	Deputy Director, OSCE, OGD, FDA
	Ed Stanley, PEng	Manager of R&D QA Compliance and Combination Products, Apotex Inc.
12:00 PM – 1:00 PM	***Lunch Break***	
Session 3:	**Other Design Differences: Justifying Differences in User Interface That May Impact an External Critical Design Attribute**	
	During comparative analyses for a proposed drug-device combination product, a generic drug manufacturer identifies user interface differences that may affect one or more critical user tasks. What are the roles of device redesign and additional information or data, such as those from comparative use human factors studies? How will OGD-funded research contribute to identifying other types of information or data that could support certain types of user interface differences?	
1:00 PM – 1:05 PM	***Introduction to Session 3***	
	Katharine B. Feibus, MD	Team Leader, Device Evaluation Team (Team D), DTP-I, ORS, OGD, FDA
1:05 PM – 1:20 PM	***Best Practices for Comparative Use Human Factors Study Design, Execution, and Reporting***	
	Jason Flint, MBA, PMP	Associate Director of Human Factors, DMEPA-I, OMEPRM, OSE, FDA
1:20 PM – 1:35 PM	***Research Efforts to Broaden Published Data on User Interface Differences & the Impact on User Error to Support Certain Types of User Interface Differences***	
	Katharine B. Feibus, MD	Team Leader, Device Evaluation Team (Team D), DTP-I, ORS, OGD, FDA
1:35 PM – 1:50 PM	***A Generic Drug Industry Perspective: Obstacles & Challenges in Device User Interface Design***	
	Claire McDiarmid, MS	Senior Director, Global Device Development, Viatris, Inc.
1:50 PM – 2:30 PM	***Q&A Session with Panel***	
Moderator:	**Katharine B. Feibus, MD**	Team Leader, Device Evaluation Team (Team D), DTP-I, ORS, OGD, FDA
Panelists:	**Jason Flint, MBA, PMP**	Associate Director of Human Factors, DMEPA-I, OMEPRM, OSE, FDA
	Claire McDiarmid, MS	Senior Director, Viatris Global Development, Viatris, Inc.
	CAPT Irene Z. Chan, PharmD	Deputy Director, OMEPRM, OSE, FDA
	Somesh Chattopadhyay, PhD	Lead Mathematical Statistician, DB-VIII, OB, OTS, FDA
	William Chong, MD	Director, OSCE, OGD, FDA
	Markham Luke, MD, PhD, FAAD	Director, DTP-I, ORS, OGD, FDA
	Nitesh Patel, MPharm	Senior Manager-Regulatory and Business Continuity, Sun Pharmaceutical Industries Limited
2:30 PM – 2:45 PM	***Coffee Break***	
Session 4:	**Drug-Device Combination and Design Differences Related to Quality and Performance**	
	This session will discuss scientific and regulatory considerations, challenges, and best practices related to the quality and performance of generic drug-device combination products and product design differences.	
2:45 PM – 2:50 PM	***Introduction to Session 4***	
	Jamie Michalek, PhD	Senior Pharmaceutical Quality Assessor, DLBP-II, OLDP, OPQ, FDA
2:50 PM – 3:05 PM	***Current Regulatory Perspective for Demonstrating the Quality and Performance of Proposed Generic Versions of Transdermal Systems, Intravaginal Systems, Implants, and Intrauterine Systems***	
	Meenal Chavan, PhD	Senior Pharmaceutical Quality Assessor, DIMRP-III, OLDP, OPQ, FDA

3:05 PM – 3:20 PM	***Lessons Learned & Best Practices for Demonstrating the Quality and Performance of Proposed Generic Versions of Injectable Combination Products***	
	CAPT. Alan Stevens. MEng	Assistant Director, DHT-IIIC, OHT-III, OPEQ, CDRH, FDA
3:20 PM – 3:35 PM	***A Generic Drug Industry Perspective: Industry's Challenges with Device Development and Demonstration of Quality and Performance of Generic Drug-Device Combination Products***	
	Rakesh Khilwani, PhD	Principal Device Development Engineer, Teva Pharmaceuticals USA Inc.
3:35 PM – 4:15 PM	***Q&A Session with Panel***	
Moderator:	**Jamie Michalek, PhD**	Senior Pharmaceutical Quality Assessor, DLBP-II, OLDP, OPQ, FDA
Panelists:	**Meenal Chavan, PhD**	Senior Pharmaceutical Quality Assessor, DIMRP-III, OLDP, OPQ, FDA
	CAPT. Alan Stevens, MEng	Assistant Director, DHT-IIIC, OHT-III, OPEQ, CDRH, FDA
	Rakesh Khilwani, PhD	Principal Device Development Engineer, Teva Pharmaceuticals USA, Inc.
	Robert Berendt, PhD	Branch Chief, DIMRP-III, OLDP, OPQ, FDA
	Ashley Boam, MSBE	Director, OPPQ, OPQ, FDA
	Monica Garcia, PhD	Assistant Director, THT-IIIB1, DHT-IIIB, OHT-III, OPEQ, CDRH, FDA
	Yili Li, PhD	Senior Pharmaceutical Quality Assessor, OLDP, OPQ, FDA
	Ripen Misri, PhD	Director, Co-Development, Global R&D, Apotex, Inc
4:15 PM – 4:25 PM	***Summary of Sessions & Closing Comments for Online Attendees***	
	Markham Luke, MD, PhD, FAAD	Director, DTP-I, ORS, OGD, FDA
4:25 PM – 4:40 PM	***Coffee Break & Networking for In-Person Attendees***	

Session 5: **A Drug-Device Combination Product Development Simulation (an Enhanced Learning Experience for In-Person Attendees Only).** This highly interactive in-person experience will simulate the process of developing a drug-device combination product. In-person attendees will join industry representatives and FDA staff in exercises simulating the development of a mock complex generic drug-device combination product. During this experience, in-person attendees will:

- Actively participate in identifying development challenges and working through solutions.
- Explore human factors considerations during device development or selection.
- Take advantage of the opportunity to handle and manipulate approved and cleared devices with different design features.
- Decide when and how to use available pre-ANDA submission processes and how to respond to FDA feedback efficiently and effectively.
- Consider how the preparation for this mock ANDA submission and review process can inform future ANDA submissions for complex generic drug-device combination products.

4:40 PM – 6:00 PM	**Introduction to Session 5**	
	Betsy Ballard, MD	Medical Officer on Team D, Device Evaluation Team, DTP-I, ORS, OGD, FDA
Moderators:	**Kimberly Witzmann, MD**	Deputy Director, OSCE, OGD, FDA
	Ifeanyi U. Uwemedimo, PhD	Senior Scientific Reviewer, OCP, OCPP, OC, CDRH, FDA
	Kristina Lauritsen, PhD	Combination Product Policy Advisor, PJO, OGD, FDA
	Tzach Bachar, MS	Director, Regulatory Affairs, Padagis Israel Pharmaceuticals Ltd
	Brandon Wood, BS	Director, Regulatory Affairs, Gx Steriles, Teva Pharmaceuticals USA Inc.
	Mitul Patel, BPharm, MPharm	Senior Manager – Regulatory and Business Continuity, Sun Pharmaceutical Industries Limited
	Satyashodhan Patil, BE, PGDIBO	Deputy General Manager (R&D), Device Development, Sun Pharmaceutical Industries Limited
	Katharine B. Feibus, MD	Team Leader, Device Evaluation Team (Team D), DTP-I, ORS, OGD, FDA
	Jason Flint, MBA, PMP	Associate Director of Human Factors, DMEPA-I, OMEPRM, OSE, FDA
	Claire McDiarmid, MS	Senior Director, Viatris Global Development, Viatris, Inc.
	Ripen Misri, PhD	Director, Co-Development, Global R&D, Apotex Inc.
	Yili Li, PhD	Senior Pharmaceutical Quality Assessor, OLDP, OPQ, FDA
	Meenal Chavan, PhD	Senior Pharmaceutical Quality Assessor, DIMRP-III, OLDP, OPQ, FDA
	Michelle Lin, MD	Senior Physician, DCR, OSCE, OGD, FDA
	Viral Jogani, MPharm, PhD	General Manager (R&D) – FR&D, Sun Pharmaceutical Industries Limited
	P, Srinivas Naidu, MEng	Senior General Manager (R&D) – Packaging and Medical Devices, Sun Pharmaceutical Industries Limited

Appendix of Abbreviations

ANDA	Abbreviated New Drug Application
BCPS	Board of Pharmacy Specialties
BE	Bioequivalence
BE	Bachelor of Engineering
CAPA	Corrective and Preventive Actions
CAPT	Captain
CDER	Center for Drug Evaluation and Research
CDRH	Center for Devices and Radiological Health
CRCG	Center for Research on Complex Generics
BS	Bachelor of Science
DB VIII	Division of Biometrics VIII
DCR	Division of Clinical Review
DDCP	Drug Device Combination Products
DHT IIIC	Division of Health Technologies 3C
DHT IIIB	Division of Reproductive, Gynecology, and Urology Devices
DIMRP III	Division of Immediate and Modified Release Products III
DLBP I	Division of Liquid Based Products I
DLBP II	Division of Liquid Based Products II
DMEPA I	Division of Medication Error Prevention and Analysis I
DPD	Division of Policy Development
DTP I	Division of Therapeutic Performance I
ESQ	Esquire
FAAD	Fellow of the American Academy of Dermatology
FDA	United States Food and Drug Administration
FR&D	Formulation Research and Development
GDUFA	Generic Drug User Fee Amendments
JD	Juris Doctor
Ltd.	Limited
MD	Doctor of Medicine
MEng	Masters in Engineering
MPharm	Masters of Pharmacy
MSBE	Master of Science in Biomedical Engineering
MS	Master of Science
OB	Office of Biostatistics
OC	Office of the Commissioner
OCP	Office of Clinical Pharmacology
OCPP	Office of Clinical Policy and Programs
OCPR	Ombudsman and Conflict Prevention and Resolution
OEP	Office of Executive Programs
OGD	Office of Generic Drugs
OHT III	Office of Health Technologies 3
OLDP	Office of Lifecycle Drug Product

OMEPRM	Office of Medication Error Prevention and Risk Management
OPEQ	Office of Product Evaluation and Quality
OPQ	Office of Pharmaceutical Quality
OPPQ	Office of Policy for Pharmaceutical Quality
ORS	Office of Research and Standards
OSCE	Office of Safety and Clinical Evaluation
OSE	Office of Surveillance and Epidemiology
OTS	Office of Translational Sciences
PGDIBO	Postgraduate Diploma in International Business Operation
PGY1	Postgraduate Year 1
PharmD	Doctor of Pharmacy
PhD	Doctor of Philosophy
PJO	Product Jurisdiction Officer
PGRS	Physician Quality Reporting Initiative
QA	Quality Assurance
PLM	Product Life Management
R&D	Research and Development
RLD	Reference Listed Drug
THT IIIB1	Obstetrical and Reproductive Health Devices Team