COMBINATION PRODUCTS: MARKET TRENDS AND REGULATORY CONSIDERATIONS

DRUG DELIVERY LEADER

INTRODUCTION

Tom von Gunden
Chief Editor, Drug Delivery Leader

Across therapeutic areas, products combining a drug and a device (or any other combination) constitute a significant avenue for increased patient adherence and, therefore, overall efficacy. Along with the rise in combination products come questions and factors regarding regulatory approval for applying these technical advances to various routes of administration.

To offer a range of perspectives on the combination product market and related regulatory considerations, we gathered recent insights from various experts. First up, we get a research-based view of where the market is heading from insightSLICE principal consultant Aditi Shivarkar.

Diving into approaches to regulatory approval for combination products are three expert contributors. Consultant and professor Tim Sandle offers his take on key takeaways from FDA's guidance on addressing human factors during product design. Consultant Fran DeGrazio offers recommendations for applying a truly integrated product development approach along the way of satisfying both FDA and EU. Also on the regulator front is the final piece – a tips-oriented tutorial from Tom KraMer of design consultancy Kablooe Design.

Taken as a whole, this collection paints a vivid picture of the combination products opportunity landscape while identifying keys to traversing it successfully from a regulatory standpoint.

TABLE OF CONTENTS

GLOBAL MARKET TRENDS FOR DRUG–DEVICE COMBINATION PRODUCTS

Aditi Shivarkar
Principal Consultant at insightSLICE

Drug–device combination products, also known simply as combination products, are therapeutic or diagnostic products that combine drugs or biologics (such as vaccines or blood products), and a medical device into a single entity. The field's wide range of applications include drug-eluting stents, prefilled syringes with medications, inhalers with drugs, and transdermal patches with therapeutic agents, among others.

These products are designed to provide a more integrated and effective approach to patient care by combining the benefits of both drugs and medical devices in a single treatment, improving treatment effectiveness, enhancing patient compliance, and streamlining healthcare delivery.

The global drug-device combination products market was valued at $109.17 billion in 2022 and is estimated to be around $117.93 billion by the end of 2023. Furthermore, it is expected to reach $236.36 billion by 2033 at a CAGR of 7.2%, according to our new market research. Let's look at the three largest growth drivers, segment analysis, and geographic insights.

3 GROWTH DRIVERS OF COMBINATION PRODUCTS GLOBALLY

Advancements in Technology and Medical Innovation

One of the primary driving factors behind the growth of the global drug-device combination products market is the continuous advancements in technology and medical innovation. As researchers and healthcare companies strive to develop more effective and patient-friendly treatment options, they are increasingly exploring the potential of combining drugs and medical devices. These innovations have led to the creation of novel combination products that offer enhanced therapeutic benefits, improved drug delivery mechanisms, and better patient outcomes. From smart inhalers and drug-eluting stents to wearable devices that deliver medications, the integration of cutting-edge technologies with pharmaceuticals is reshaping the landscape of healthcare, driving the demand for drug-device combination products worldwide.

Growing Prevalence of Chronic Diseases

The rising prevalence of chronic diseases, such as cardiovascular disorders, diabetes, respiratory illnesses, and cancer, is another key driver of the global drug-device combination products market. These conditions often require long-term and targeted treatments involving both drugs and medical devices to manage symptoms effectively, control disease progression, and enhance patient quality of life. Combination products offer a valuable solution by providing a streamlined approach to therapy, reducing the need for multiple interventions, and ensuring better patient compliance.

Regulatory Support and Expedited Approval Processes

The development and approval process for drug-device combination products can be complex, as it involves the regulatory requirements for both drugs and medical devices. The responsibility for reviewing and regulating combination products often falls under a collaboration between different regulatory agencies, such as the U.S. FDA's Center For Devices & Radiological Health (CDER) and Center For Biologics Evaluation and Research (CBER) and/or Center for Drug Evaluation and Research (CDER). Governments and regulatory agencies around the world have recognized the potential benefits of drug-device combination products and have shown increasing support for their development and commercialization. Efforts to streamline the regulatory pathways and provide clearer guidelines for combination products have facilitated faster approval processes, encouraging pharmaceutical and medical device companies to invest in this market segment. Expedited approval pathways, such as the FDA's Combination Product Agreement Meetings and the European Medicines Agency's (EMA) Scientific Advice for Combination Products, have

incentivized innovation in this field. The regulatory backing and simplified approval processes have not only accelerated market entry for new combination products but have also encouraged collaborations between drug and medical device manufacturers, fostering a dynamic and competitive market landscape.

WHICH PRODUCT SEGMENT HOLDS THE LARGEST SHARE?

Based on product type, the market is segmented into:

- drug-eluting stents,
- infusion pumps,
- photodynamic therapy,
- antimicrobial wound dressings,
- prefilled syringes,
- drug-eluting balloons,
- nebulizers,
- inhalers,
- transdermal delivery systems, and
- other products.

Among these, drug-eluting stents have been one of the largest segments in the drug-device combination products market. These stents are used in interventional cardiology to treat coronary artery disease by propping open narrowed or blocked arteries and slowly releasing drugs to prevent restenosis (re-narrowing). The prevalence of cardiovascular diseases, such as coronary artery disease, has been substantial globally, and drug-eluting stents have become a standard treatment option due to their ability to reduce the chances of repeat blockages.

THERAPEUTIC INDICATIONS

Based on indication, the market is segmented into:

- cardiovascular disorders,
- diabetes,
- respiratory problems,
- cancer treatment,
- antimicrobial application, and
- other indications.

Among these, the cardiovascular disorders segment holds the largest market share for combination products. Cardiovascular diseases, such as coronary artery disease, heart failure, and arrhythmias, have been among the leading causes of morbidity and mortality worldwide for several years. Combination products play a crucial role in the treatment of cardiovascular disorders, with examples such as drug-eluting stents, pacemakers with drug delivery capabilities, and implantable defibrillators.

GEOGRAPHIC MARKET TRENDS

Geographically, the global drug-device combination products market is segmented into North America, Europe, Asia-Pacific, Middle East and Africa, and South America, with North America being largest segment. This is primarily due to several factors:

- North America, especially the United States, is home to a robust and innovative healthcare industry, including both pharmaceutical and medical device sectors. This fosters a conducive environment for research, development, and commercialization of drug-device combination products.
- The region has a large patient population with a significant prevalence of chronic diseases, creating a substantial demand for integrated and advanced treatment options.
- North America's regulatory agencies, such as the U.S. FDA, have been proactive in supporting the development of combination products, offering expedited approval pathways and clear guidelines.
- North America is also seeing a rise in telehealth and remote patient monitoring, leading to higher demand for connected drug-device combination products.

In Europe, there's a surge in demand for wearable combination products and smart delivery systems, with many market players investing in digital health technologies to enhance treatment outcomes.

In the Asia-Pacific region, there's a shift toward self-administration devices and targeted drug delivery systems. There is also an increasing number of collaborations between global and local companies to address market needs.

The key players of the global drug-device combination products market are:

- Abbott Laboratories (U.S.)
- Baxter International Inc. (U.S.)
- Bayer AG (Germany)
- Becton, Dickinson and Company (U.S.)
- Boston Scientific Corporation (U.S.)
- GlaxoSmithKline plc (United Kingdom)
- Johnson & Johnson (U.S.)
- Medtronic plc (Ireland)
- Novartis International AG (Switzerland)
- Smith & Nephew plc (United Kingdom)

ABOUT THE AUTHOR:

Aditi Shivarkar is principal consultant at insightSLICE, a market intelligence and strategy consulting company. She has been a part of the research industry for 13 years. She joined insightSLICE in 2021 and she works with clients to design studies that generate the data needed to answer their strategic market analysis, segmentation, brand equity, and pricing questions. She works across various domains, including healthcare, industrial automation, consumer goods, IT, and telecom.

FDA RELEASES Q&A GUIDANCE ON HUMAN FACTORS ENGINEERING FOR COMBINATION PRODUCTS

Tim Sandle, Ph.D.

Author And Consultant To The Pharmaceutical Industry

Human factors engineering involves the design of objects and systems by accounting for human capabilities, limitations, and characteristics. Applied to pharmaceuticals, the goal would include designing products for safe, effective, and comfortable human use, and it answers questions like “how easily can a person use this medicine?”

When outlining the application of optimal design principles, human factors are often subdivided into physical, cognitive, social, cultural, and emotional factors. By working through these subfactors and appropriately validating combination products, human factors engineering aids personnel in analyzing patient safety events and in developing workable and effective countermeasures.

An important component of pharmaceutical products and medical device research and development is a focus on the users of the device. Developing an effective device or medication can be easily undone if it is not used correctly, and errors made by patients or clinicians are often a direct result of design limitations.[1] Weaknesses can be overcome by focusing on human factors, undertaken through a process of iterative design and testing and supported by measuring and analyzing the interactions between people and medicines.[2] One area where errors can occur is combination products. These are medicines that contain two or more separate products packaged together in a single package, or they are provided as a unit comprising a drug and a device, a device and a biological product, or biological and drug products. Examples of combination products are the emerging set of digital health products that include digital interfaces, and which are designed to collect data.

To support the co-packaged design process, the U.S. FDA has issued a new guidance document, in the form of a Q&A, titled Application of Human Factors Engineering Principles for Combination Products: Questions and Answers.[3] In this article, I review some of the pertinent points from the guidance.

EMPHASIS ON QUALITY RISK MANAGEMENT

As with most recent FDA guidances, the document emphasizes risk management. There are risks associated with the device, use-related risks associated with the medicine, and use-related risks associated with the combination product as a whole, beyond those that arise from using either the device or drug alone.[4] The use-related risks are expanded upon in the FDA document, particularly regarding the user interface and the need for a human factors engineering assessment.

The user interface includes all points of interaction between the combination product and the user(s), including displays, controls, packaging, product labels, carton labeling, and instructions for use. In addition, this may need to include training for the patient or clinician, if applicable.[5]

The guidance discusses different levels of risk. The most serious of these is described as a "combination product critical task." This is a task undertaken by the user which, if performed incorrectly or missed, could cause compromised medical care. For example, a freeze-dried product requires reconstituting using a liquid, and this must be completed within a certain time frame, with the objective of providing a homogenous solution. If the patient is unable to complete the task within the time frame due to the product design or a characteristic of the product (such as the product not dissolving fast enough), this would represent a product critical task.

The important points to consider in the human factors engineering risk assessment include:

- A sufficient knowledge about human behavior, abilities, and limitations, together with other characteristics relating to the intended the users of the products, must be built. This requires an understanding of the intended user population, including concomitant diseases and conditions.
- Limitations extending from specific health conditions that could impact the use of the combination product need to be accounted for.
- General health factors need to be considered. The FDA document provides an example relating to digital technology: If the intended patient is classed as geriatric, then the images and sounds need to be suitably clear and supported by intuitive technology. It may also be necessary to consider how a product might be used by a person undergoing cognitive decline.
- For other patient groups, varying literacy levels need to be understood.
- The location where the product is to be used will need to be assessed, including any limitations connected to two-way communication and data transmission. For example, products designed to transmit data may not perform where there is only limited internet access or disrupted cellular services.
- Consider how the design of the user interface affects interactions with the combination product and could potentially result in harm, including a medication error.

The FDA guidance expands the risk-based approach to consider some specific hazards, as noted below.

Injectable Products

One of the risk areas considered includes devices that inject a medication into the patient. The first human factors area addressed is pain. If pain is considerable, then this carries the potential for the user not to complete the injection task. This could lead to dose omission or at least an underdose.

A second factor with injectable medicines is the viscosity of the product. A high drug viscosity could increase the injection delivery time of the drug through the needle; in turn, this could increase the length of time the user needs to hold the injector in place to deliver the medicine. A prolonged hold time could also reduce the user's ability to complete an injection task and again result in an underdose. This could arise, for example, if a needle needs to be fully depressed prior to injection, but the instruction to the patient that the needle needs to be fully depressed is not clear.

Direct Harm

Another risk area is a combination product with the potential to result in harm, such as causing physical injury, adverse events; events that need patient monitoring to confirm no harm occurred; or events that may lead to hospitalization. Each of these potential outcomes should be modeled and the associated risks reduced.

To avoid such harm, the concepts of a device being error-resistant and error-tolerant can be introduced.6 These terms

are not explicitly used in the guidance, but they are useful to keep in mind. "Error-resistant" means that, as far as possible, the design should protect users from making errors. "Error-tolerant" infers the design should minimize the consequences of any human errors that are committed.

Site Of Administration

The design of the device and the instructions must be sufficiently clear so that the administration impact of the product is reduced. Problems that could arise include the patient targeting the wrong site of administration as well as improper preparation of the medicine prior to administration.

Route Of Administration

Instructions about the route of administration need to be clear. For instance, if a capsule is provided with an inhaler, it cannot be assumed that the patient knows to place the capsule in the inhaler and for the medication to be delivered by inhalation. If the patient was to simply swallow the capsule, the medication would be ineffective (and possibly dangerous) due to the incorrect route of administration being selected.

Time Delays

The design of some combination products may lead to time delays. For example, if a patient is required to administer one dose of a product followed by a dose of a second product within a short time frame, then something like the cap of a vial being difficult to remove presents a human factors problem since this could delay the patient getting the second dose ready within the required time frame. On the other hand, if the two doses are not time dependent, additional time to remove a cap will matter less.

VALIDATION

The FDA guidance emphasizes the importance of including the use of the combination product within the validation exercise for assessing the pharmaceutical product. It is necessary to evaluate users' interactions with the final finished combination product across different scenarios. To support any future changes, the reassessment of validation forms an important part of the change management process.

ROOT CAUSE ANALYSIS

The human factors approach also can be applied to root cause analysis. This is not addressed in the FDA guidance, but it is a useful adjunct. Instead of thinking why the people involved are so "odd" as to "misuse" a product, the human factors approach should drive companies to understand why the patients' decisions and actions make sense and to incorporate this insight into continuous improvement practices.

REFERENCES

1. *Dakken S. Field guide to human error investigations. Burlington, VT: Ashgate Publishing Co, 2002*
2. *Battles JB, Keyes MA. Technology and patient safety: A two-edged sword. Biomedical Instrumentation & Technology. 2002;36(2):84–88*
3. *FDA. Application of Human Factors Engineering Principles for Combination Products: Questions and Answers, Guidance for Industry and FDA Staff, Office of Combination Products: https://www.fda.gov/media/171855/download*

4. *Panagioti M, Khan K, Keers RN, et al. Prevalence, severity, and nature of preventable patient harm across medical care settings: systematic review and meta-analysis. BMJ 2019; 366:l4185*
5. *Welch DL. Human error and human factors engineering in healthcare. Biomed Instrum Technol.,1997;31:627–31*
6. *Implementing Human Factors in Healthcare: How to guide (volume 2): http://www.institute.nhs.uk/images/documents/SaferCare/Human-Factors-How-to-Guide v1.2.pdf*

ABOUT THE AUTHOR

Tim Sandle, Ph.D., is a pharmaceutical professional with wide experience in microbiology and quality assurance. He is the author of more than 30 books relating to pharmaceuticals, healthcare, and life sciences, as well as over 170 peer-reviewed papers and some 500 technical articles. Sandle has presented at over 200 events and he currently works at Bio Products Laboratory Ltd. (BPL), and he is a visiting professor at the University of Manchester and University College London, as well as a consultant to the pharmaceutical industry. Visit his microbiology website at https://www.pharmamicroresources.com.

YOUR BEST CHANCE AT REGULATORY COMPLIANCE FOR COMBINATION PRODUCTS: INTEGRATED DEVELOPMENT

Fran DeGrazio
Principal Consultant At
Strategic Parenteral Solutions LLC

The near-term future of combination products continues to be the growth of prefillable syringe systems (PFS) and their use in autoinjectors (AI), especially due to the trend toward self-administration. Per Vantage Market Research, the global prefilled syringe market is projected to reach a value of $10.59 billion by 2030. This correlates to a CAGR of 8.70% from 2023 to 2030.

One recent example of this trend toward self-administration is the injectable monoclonal antibody belimumab, which is used to treat active autoantibody-positive systemic lupus erythematosus and active lupus nephritis in patients who are receiving lupus treatments. Originally approved by the FDA in 2011, the medicine is currently available in three forms: a vial/stopper/seal glass container system, a prefilled glass syringe, and an autoinjector (with prefilled syringe), with the autoinjector being approved by the FDA in 2017. Both the prefilled syringe and auto injector versions can be used in the home setting. This is only one example of many biologic drugs provided in similar formats.

The coming together of the drug with its packaging and its delivery system brings with it some of the greatest challenges for manufacturers from a technical and regulatory standpoint. As presented in 21 CFR Part 4, a combination product is composed of two or more different types of medical products. Several U.S. regulatory documents, including the FDA Guidance for Industry and FDA staff: Current Good Manufacturing Practice Requirements for Combination Products, published in January 2017, clearly present prefilled syringes and prefilled syringes in autoinjectors as combination products.

In Europe the regulatory framework for medical devices, Regulation (EU) 2017/745, explains that systems marketed as a single integral product intended exclusively for use in the given combination and that are not reusable are governed by the medicinal products framework. For PFS, this means the relevant general safety and performance requirements (GSPRs) of Annex 1 of the MDR (Medical Device Regulations) must be met.

INTEGRATING DRUG AND DEVICE CGMP

The FDA now defines a prefilled syringe, a product that was at one point considered "packaging" for a drug, as a constituent part of a combination product. The ultimate combination of the drug, its package, and its delivery device means that during development and manufacturing there is a need to combine both drug and device current good manufacturing practices (cGMPs) and quality approaches, even though prefillable syringes may be considered a "commodity" product by those who are less familiar (i.e., non-technical/non-regulatory professionals).

QbD And Design Controls

In the past, meeting the drug GMPs was the minimum needed for regulatory approval. Through the years, however, best practices that build on this foundation have been developed. A best practice expectation now is to develop a new drug from a risk-based perspective. The driver behind this was the release of documents such as ICH Q8 R2 (Pharmaceutical Development), ICH Q9 (Quality Risk Management), ICH Q10 (Pharmaceutical Quality System), ICH Q11 (Development & manufacture of drug substances), and ICH Q12 (Technical & Regulatory considerations for pharmaceutical product lifecycle management). These guidances form the foundation for quality by design (QbD) in drug development and commercialization. QbD employs a risk-based approach that improves product and process understanding through building knowledge via statistical and analytical approaches. Quality is built in from the beginning of the development process. It is, in essence, the drug version of design controls for medical devices.

Terminology is different between QbD and design controls, so this becomes part of the challenge in working to develop a combination product. You are truly bringing together science and engineering in a way that has not been done in the past.

Through QbD, you build a design space that is focused on robustness. A complete picture allows the understanding of the product and process so process analytical technology (PAT) can be leveraged within manufacturing. All this development and understanding should tie to a robust control strategy that applies to both the drug and the device portions of the combination product.

21 CFR Part 4 – Regulation of Combination Products does make it clear that the applicable parts of the drug and device regulations must be met. The translation from regulation to practice and how that applies to the total combination product are the issues.

The challenge in the recent past is that while QbD and design controls have been established for some time for drugs and devices, how they apply to the total combination product has not. Best practices and guidance continue to be developed in this space, with varying amounts of knowledge and experience across the industry.

Essential Performance Requirements

Since PFS is now deemed a combination product, the functional aspects of delivery are as important as the chemical aspects of the package itself. Essential performance requirements (EPRs) or primary functions (PF) become extremely important to characterize and identify during development. Prefilled syringes have the benefit of having a commonly accepted ISO standard used as a reference. This standard, ISO 11040-8: Prefilled Syringes, connects back to a series of normative references that allow you to best identify the testing needed for the specific drug product and patient application. The FDA is to release an EPR guidance by the end of 2023 that should provide more elucidation around the terminology and requirements. Of course, the guidance, coupled with the risk-based development process, should inform the choices made throughout the process.

Prefilled syringes in autoinjectors follow this same path of understanding. Currently, the FDA considers EPRs as attributes responsible for the clinical performance of the delivery system at point of dosing, including those required to administer the dose. This is very similar to the concept of "primary functions" as designed in ISO 11608-1:2022 Needle-based injection systems for medical use.

Although a platform approach may be taken by companies working on multiple drug products that are delivered by a prefilled syringe and an autoinjector, it is important to understand and characterize each piece of the platform while understanding that the requirements for the design inputs and target product profile should be unique and well understood for the specific therapeutic category, patient group, and user group.

The FDA Draft Guidance Bridging for Drug-Device and Biologic-Device Combination Products (published in December

2019) provides direction on how to leverage data that may have been generated in another development program to support a new application. Utilizing risk analysis to understand what data can be used is a key part of this process.

During development, when setting up the user needs and target product profile, form, fit, and function should be considered. This includes the typical requirements of a drug or biologic from a stability standpoint plus considerations around protection, compatibility, and performance of the device. Additionally, these pieces cannot be taken separately as the fit between the primary package and the device/delivery system can be a key source of potential problems if not understood and controlled effectively.

The proactive engagement of drug, packaging, and device subject matter experts during the chemistry, manufacturing & controls (CMC) process will help to minimize development or post-market problems.

CONCLUSION

This article only touches on the very significant challenge of delivering combination products to patients in an efficient manner. A deep dive is needed for anyone engaging in active development and commercialization of these products.

Innovation of syringes and autoinjectors continues. This means even more new challenges from a technical and regulatory perspective. Examples of this are the addition of digital/software capabilities, an increase in the volume that the systems can deliver, and the addition of new aspects such as gas-powered systems, to name a few. Optimization of an integrated development process that can be replicated and executed upon is the best way to assure success since combination products are the future of the industry.

ABOUT THE AUTHOR

Fran DeGrazio is a Kymanox executive advisor as well as president and principal consultant for Strategic Parenteral Solutions LLC. She has more than 35 years of experience in the pharmaceutical packaging and delivery industry, with extensive expertise in sterile drug product systems, including vial container closure systems and prefillable systems for combination products.

HOW TO MAKE THE FDA HAPPY: 7 MEDTECH DESIGN PRO TIPS FOR COMBINATION PRODUCTS

Tom KraMer

President And CEO,
Kablooe Design

The world of medical technology is ever evolving, and one significant innovation that's been gaining momentum is combination products. These remarkable medtech products seamlessly integrate both medical devices and pharmaceutical components into a single cohesive solution.

However, as the industry evolves, so do the regulatory requirements. Let's dive into the unique landscape of combination devices and explore seven pro design tips to not only meet the FDA's stringent standards but exceed them.

CONDUCTING USABILITY STUDIES

The FDA likes to see studies — and for good reason. They want to know that your combination device is both safe and effective, and this can only be demonstrated through rigorous usability studies. Make sure your team has the expertise (or partner) necessary to carry out these studies effectively.

Pro Tip #1: Know Your Goal

What are you trying to learn? You can start by gathering as much information about the combination product as you can. Then, once you know your goal, you can develop a study plan that is both efficient and informative.

Pro Tip #2: Know the Regulatory Deliverables

These can include everything from an IDE application to a 510(k) submission. According to FDA guidance, there are five major pre-validation items and two major post-validation items that need to be included in any study.

Pre-Validation Items:

- updated risk analysis from resulting design changes
- summary of formative study results/analysis
- documented design changes and rationale
- a draft of the summative study protocol
- labeling and IFU to test in the summative study

Post-Validation Items:

- summative study (validation) protocol and summary
- summary of total human factors effort

When it comes to combination devices, we have to think a bit deeper about how we will evaluate the device for usability testing. In the FDA's new guidance document, they pay special attention to use errors that might:

1. Impact dosing (e.g., an overdose, underdose, or missed dose), including those that may lead to a lack of treatment response;
2. Impact administration of the product (e.g., the wrong site of administration, improper preparation of the drug/biologic before administration); or
3. Have the potential to result in harm (e.g., physical injury, adverse events, events that may need patient monitoring to confirm no harm, or events that may lead to hospitalization).

Making sure we understand what the users are capable of in these areas, what they are likely to do (and not do), and how we can improve our designs to make it easier for them are all important things for us to consider when designing the features and functions of the combination device.

Pro Tip #3:
Conduct Your Summative Studies BEFORE Your Large Clinicals

This is more of a general guideline than a hard rule, as even the FDA acknowledges that there are exceptions to this order.

DESIGN CONTROLS

All combination products must undergo a rigorous design control process, which helps catch and correct potential problems, ensuring your product is safe and effective. The FDA has outlined specific design control requirements in Section 820.30 of their Quality System Regulation (QSR), and it's important to adhere to these if you want your product to get approval. Think of this as a sort of guideline for all your development activities leading up to production.

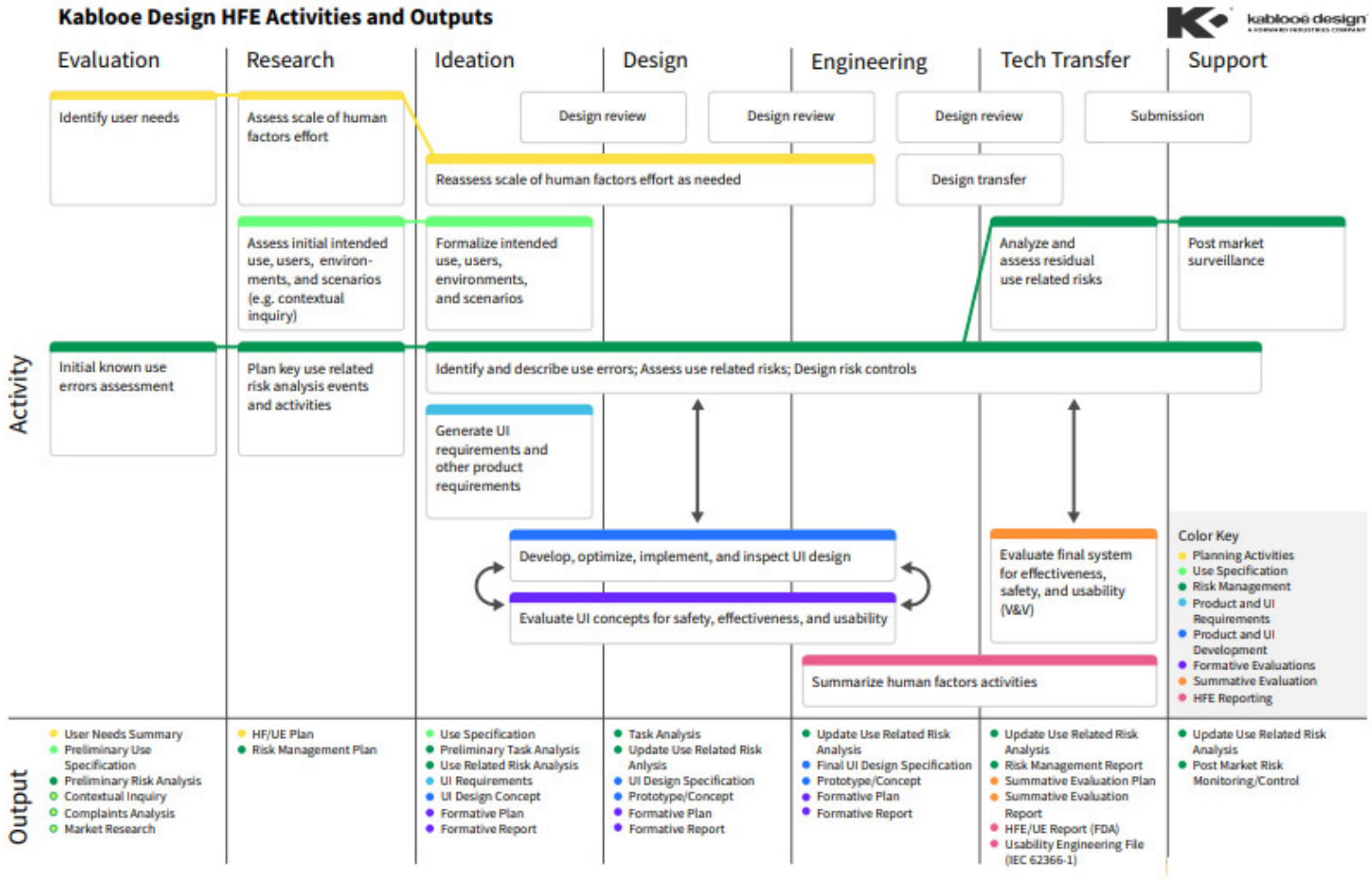
Pro Tip #4:
Properly Manage Your Design Controls

The key to any successful design control process is clear documentation, organization, and communication. Make sure all team members are on the same page by creating concise documentation that's understood by all. It's also important to use a good software tool to manage your design controls. This will make it easier to track changes, ensure compliance with regulations, and generate accurate reports.

THE HUMAN FACTORS ENGINEERING PLAN

A human factors engineering (HFE) plan will help you think through how people will use your combination device in the real world and can help you avoid costly redesigns down the road. By integrating HFE activities into development at the start, you can mitigate a ton of issues that could pop up at the worst possible time.

A portion of this work will be covered in your design controls, which are governed by previously cited guidance documents, as well as the Association for the Advancement of Medical Instrumentation (AAMI) TIR59:2017.


Kablooe Design HFE Activities and Outputs
kablooe design
Evaluation
Research
Ideation
Design
Engineering
Tech Transfer
Support
Activity
Identify user needs
Assess scale of human factors effort
Design review
Design review
Design review
Submission
Reassess scale of human factors effort as needed
Design transfer
Assess initial intended use, users, environ-ments, and scenarios (e.g. contextual inquiry)
Formalize intended use, users, environments, and scenarios
Analyze and assess residual use related risks
Post market surveillance
Initial known use errors assessment
Plan key use related risk analysis events and activities
Identify and describe use errors; Assess use related risks; Design risk controls
Generate UI requirements and other product requirements
Develop, optimize, implement, and inspect UI design
Evaluate UI concepts for safety, effectiveness, and usability
Evaluate final system for effectiveness, safety, and usability (V&V)
Summarize human factors activities
Color Key
Planning Activities
Use Specification
Risk Management
Product and UI Requirements
Product and UI Development
Formative Evaluations
Summative Evaluation
HFE Reporting
Output
User Needs Summary
Preliminary Use Specification
Preliminary Risk Analysis
Contextual Inquiry
Complaints Analysis
Market Research
HF/UE Plan
Risk Management Plan
Use Specification
Preliminary Task Analysis
Use Related Risk Analysis
UI Requirements
UI Design Concept
Formative Plan
Formative Report
Task Analysis
Update Use Related Risk Anlysis
UI Design Specification
Prototype/Concept
Formative Plan
Formative Report
Update Use Related Risk Analysis
Final UI Design Specification
Prototype/Concept
Formative Plan
Formative Report
Update Use Related Risk Analysis
Risk Management Report
Summative Evaluation Plan
Summative Evaluation Report
HFE/UE Report (FDA)
Usability Engineering File (IEC 62366-1)
Update Use Related Risk Analysis
Post Market Risk Monitoring/Control

Pro Tip #5:
Provide Your HFE Data BEFORE Your Summative Reports

The FDA wants to help you evaluate and form your summative protocol to make it more effective and with a higher chance of success — so let them!

Pro Tip #6: Avoid Human Factors Engineering Altogether

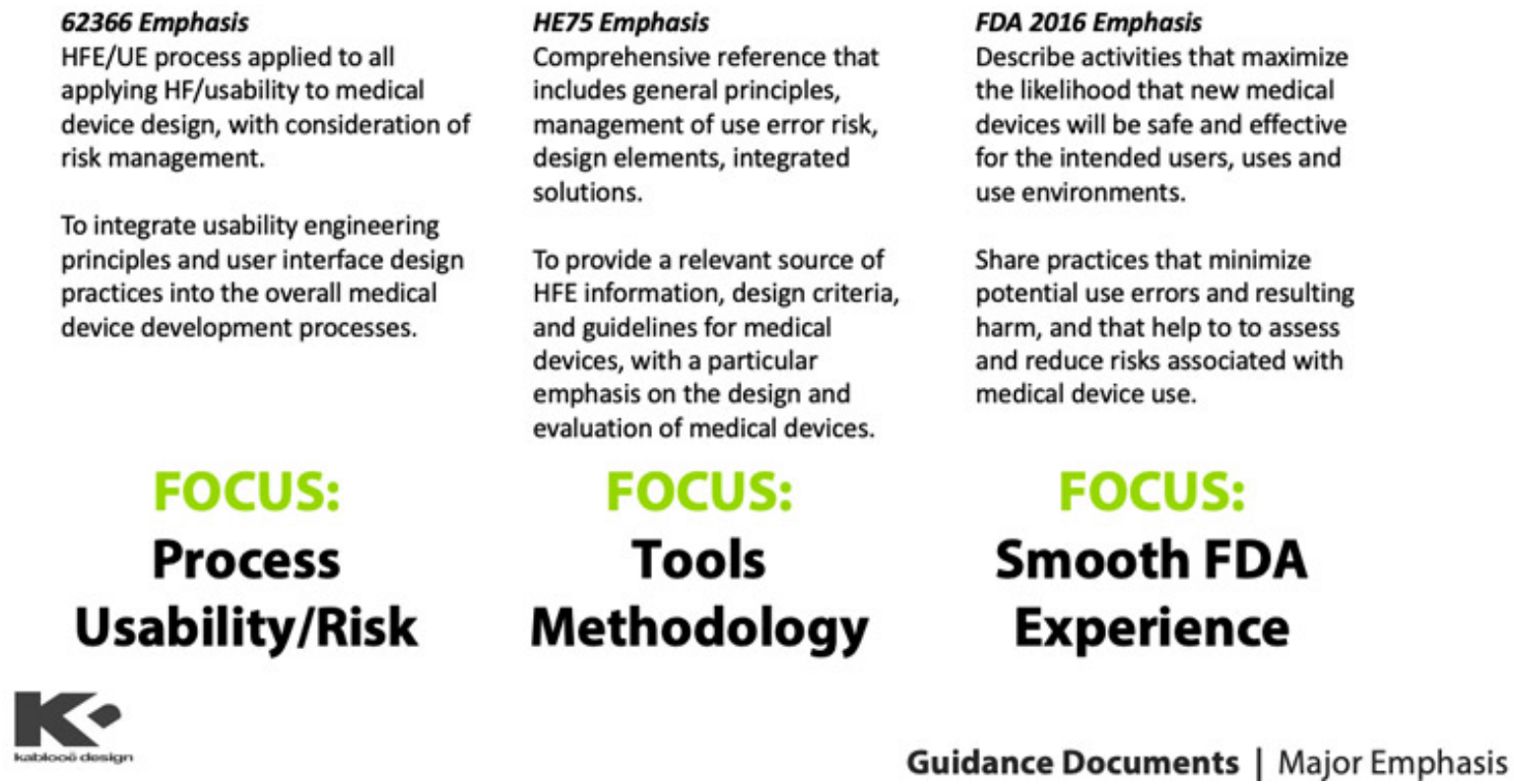
I know, this is contradictory to everything I just said. The thing is, though, if your usability risk assessment can show that HFE is not needed, you should make a good case for that and present it to the FDA. This can save you a lot of time and resources in the long run.

U.S. VS. EU MARKETS

The FDA is not the EU, but it is close. The FDA and the European Medicines Agency (EMA) have different approval processes, so it's important to understand the specific requirements of each one. Differences can include the types of studies required and the level of detail that needs to be included in your submission.

Here are some standards documents for reference:

- European and International: IEC 62366
- American National Standard: AAMI H



Pro Tip #7:
Understand the Regulatory Differences That Are Most Likely to Affect You

There are three main differences that are important enough to highlight here. Keep in mind, though, that these are general differences and not hard and fast rules. Things change fast.

The European system asks for a "User Interface Specification". The U.S. guidance describes tasks to be done but stops short of requiring a specific report for those tasks that align.

The U.S. systems seem to need to see a lot of summative preliminary work. Europe, on the other hand, is more focused on the summative report.

The U.S. system puts a lot of focus on analysis such as Use Failure Modes and Effects Analysis (uFMEA) and fault tree analysis (FTA). The purpose of a uFMEA evaluation is to assess aspects of the user interface as well as task failure effects. An FTA examines assumptions to see whether they are reasonable or if modifications should be made.

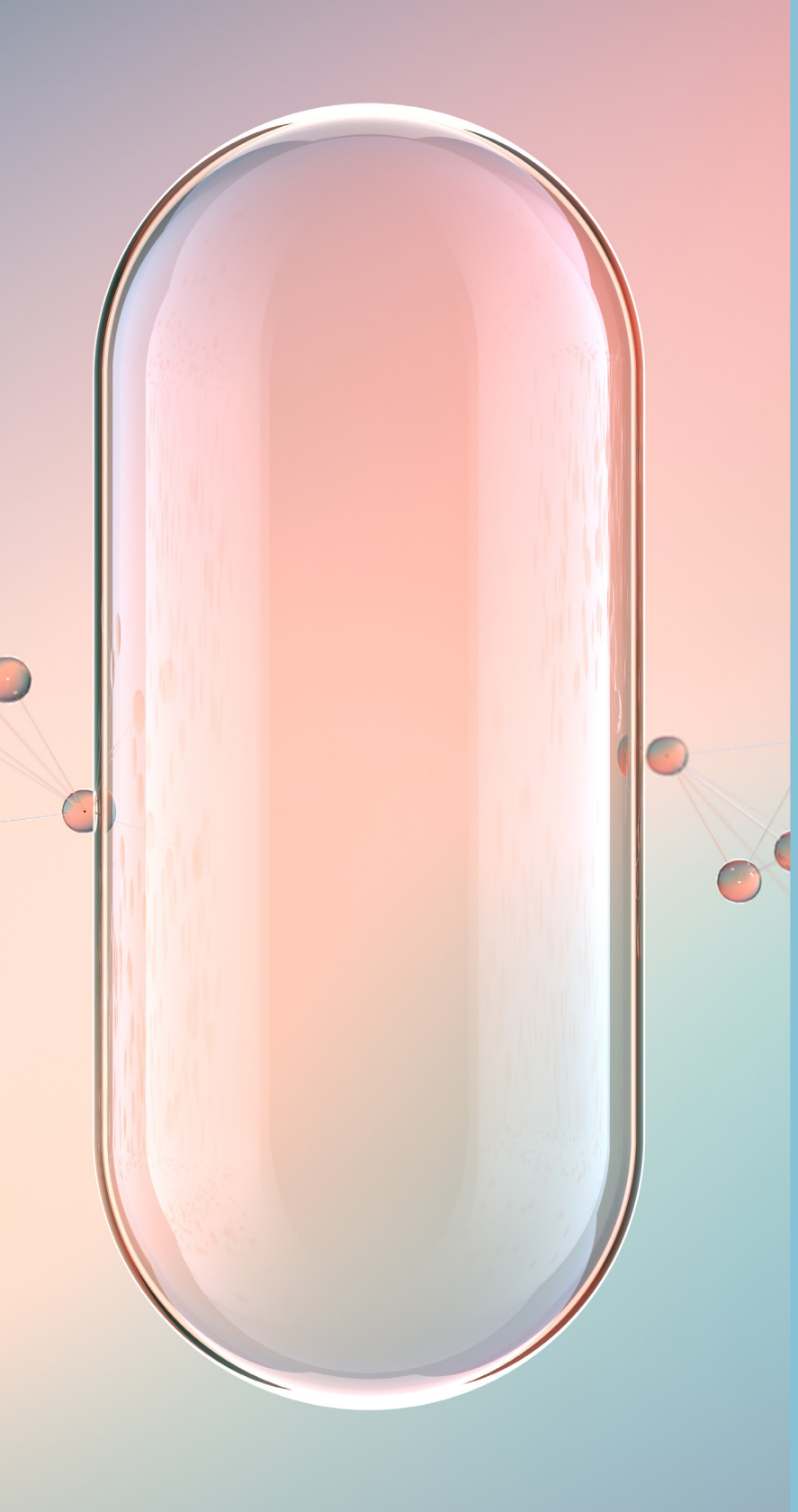
ARE YOU READY TO MAKE THE FDA HAPPY?

Sure, you are! By following these seven pro tips, you'll be well on your way to success. After all, making the FDA happy is essential for any medtech company looking to bring their combination device to market.

Want one final pro tip? Making the FDA happy isn't just about compliance — it's about elevating patient care and driving innovation in the medtech industry.

ABOUT THE AUTHOR

Tom KraMer, president and CEO of Kablooe Design, has been a product innovator for over 30 years. He holds a certificate in master of product development from Northwestern University and a bachelor's degree in industrial design from the Minneapolis College of Art and Design (MCAD), as well as a certificate from Stanford University's Cardiovascular System in Health and Disease program. KraMer has created revenue for countless customers by delivering innovative product solutions to their portfolios. He spearheaded the D3 Process (Design Driven Development), a vehicle to provide these results to customers, and he teaches this process by traveling as a lecturer and speaking about innovation and development processes.



ABOUT US

DRUG DELIVERY LEADER

Drug Delivery Leader focuses on the people, technologies, and processes responsible for optimizing the therapeutic delivery of pharmaceutical compounds. The community highlights best practices and advancements throughout the development process with respect to drug delivery, from drug formulation to the design/development and, ultimately, procurement of drug delivery solutions. Scientific and engineering professionals will gain insights into addressing the biggest challenges related to drug delivery – via injectable, oral solid dose, inhalation, infusion, transdermal, and ocular routes of administration.

DrugDeliveryLeader.com
info@DrugDeliveryLeader.com
814.897.7700
5340 Fryling Rd., Ste 100, Erie, PA 16510