DTx Product Best Practices

To demonstrate product integrity and ensure patient safety, all DTx products should adhere to Industry Core Principles.[1] These principles serve as guideposts to end users, clinicians, and payors as they assess the purpose and quality of DTx products. The associated Best Practices provide further clarity to the types of methods DTx products may use to achieve alignment with each principle.

Note: This list will continue to evolve to reflect ongoing relevancy related to DTx product design, evaluation, and deployment best practices.

CORE PRINCIPLES	ASSOCIATED BEST PRACTICES
1. **Prevent, manage, or treat a medical disorder or disease**	▪ DTx products make one of the following claims: - Treat a disease - Manage a disease - Improve a health function or prevent a disease ▪ Product claims must directly align with the: - Exact language that has been approved by a regulatory or market authorization body; OR, - Language used by a regulatory body to determine enforcement discretion (or equivalent)
2. **Produce a medical intervention that is driven by software and delivered via software or complementary hardware, medical device, service, or medication**	▪ Validate the delivery and utilization of the intervention across potential use scenarios, including supervised and unsupervised use ▪ Validate appropriateness of the selected mechanism of delivery for the software-driven medical intervention ▪ Deliver reliable interventions that align with product claims ▪ Validate accuracy and reproducibility of data intake and generation processes ▪ Validate reliability of data collection and upload processes in real-time or post-session batches ▪ Define data provenance and source traceability ▪ Ensure product is interoperable with all applicable hardware, software, service, and/or drug components (e.g., ISO/IEEE 11073)
3. **Incorporate design, manufacture, and quality best practices**	▪ Incorporate data-driven and informed interventional pathways based on validated clinical mechanisms of action ▪ Build software in accordance with consensus certifications, standards, and guidance (e.g., IEC 62304, ISO 14971, IEC 62366-1, AAMI TIR 45, IEEE P2675) ▪ Establish and adhere to Current Good Manufacturing Practices (cGMPs) for software medical devices (e.g., ISO 13485, 21 CFR 820) ▪ Utilize auditable and transparent validation methods to ensure that high standards are reliably met

1 *Digital Therapeutics: Combining Technology and Evidence-based Medicine to Transform Personalized Patient Care*. Digital Therapeutics Alliance. Oct 2018.

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4. Engage end users in product development and usability processes	▪ Design the product using a human-centered approach, accounting for the user's core needs, abilities, environments of use, and device interface (e.g., ISO 9241-210) ▪ Design product to optimize adoption, engagement, and adherence within target population ▪ Integrate product accessibility and universally-designed features where appropriate (e.g., Xcertia Guideline U9) ▪ Conduct human factors testing throughout product development and usability processes (e.g., standard operating procedure aligned with ISO 62366)
5. Incorporate patient privacy and security protections	**Patient Privacy** ▪ Comply with all applicable electronic Protected Health Information (ePHI) regulations ▪ Adhere to the most applicable good practice guideline(s) (e.g., General Data Protection Regulation (GDPR), Health Insurance Portability and Accountability Act (HIPAA)) ▪ Provide end users with a privacy notice that describes how the organization collects, uses, and retains end user data, the types of data that the product obtains, the length of data retention, and how and by whom information is used ▪ Implement measures to protect children in accordance with applicable laws and regulations if the product is directed at children (e.g., Xcertia Guideline P5) **Product Security** ▪ Pass and obtain appropriate security and vulnerability certifications, including standards-based guidelines to safeguard data at rest and in-transit through proper authentication, encryption, and other methods (e.g., SOC 2 certification, HITRUST certification) ▪ Establish robust internal security management and monitoring systems to protect any personal data that is collected, stored, or transmitted ▪ Monitor changing external security environments, with a focus on how to protect patient and end user private information ▪ Employ a system that identifies, monitors, and addresses cyber events to detect and correct problems in a timely manner ▪ Protect product integrity and proactively address cybersecurity issues through active engagement with stakeholders and peers ▪ In case of a breach, inform the relevant supervisory authority of security violations as soon as possible and communicate actions to rectify the problem and diminish future risk
6. Apply product deployment, management, and maintenance best practices	▪ Utilize an end user-focused approach for product deployment and ongoing maintenance ▪ Ensure that products are scalable across the necessary environments of use ▪ Build internal and external infrastructure to ensure sustained product availability ▪ Establish appropriate systems to manage and report, where necessary, compliance, technical, or recall issues ▪ Develop appropriate communication and technical support services to account for end user success ▪ Account for marketplace feedback, product performance data, product outcomes, and adverse events in ongoing product development efforts ▪ Conduct ongoing risk analyses and mitigation efforts throughout the product lifecycle ▪ Adhere to best practices for clinical risk management, APIs, data offshoring, and cloud services

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7. **Publish trial results inclusive of clinically-meaningful outcomes in peer-reviewed journals**	▪ Adhere to rigorous standards of clinical evidence generation, analysis, and application throughout the DTx product lifecycle ▪ Conduct one or more adequately-powered, well-controlled, fit-for-purpose clinical investigations in the target population, including a randomized control trial (RCT), to: - Demonstrate medical evidence of benefit and safety - Establish valid association between DTx product outputs and the targeted clinical condition - Verify ability of DTx product to correctly process input data and generate accurate, reliable, and precise output data - Verify ability of DTx product to achieve intended purpose in target population in the context of clinical care ▪ Receive approval for structured clinical studies by an institutional review board and register in a clinical trials registry before study begins, appropriate to clinical claims ▪ Ensure transparency of study and control arm design, statistical analysis, and results ▪ Demonstrate statistically significant results on the primary outcome(s) and/or study endpoint(s) ▪ Publish trial results inclusive of clinically-meaningful outcomes on the stated primary outcome in peer-reviewed journals
8. **Be reviewed and cleared or approved by regulatory bodies as required to support product claims of risk, efficacy, and intended use**	▪ Comply with oversight provided by each applicable regulatory agency and/or notified body ▪ Register with the applicable regulatory agency and/or notified body in each jurisdiction where the product is used and comply with all manufacturing requirements ▪ Undergo a risk-based assessment by bodies responsible for market authorization when appropriate to evaluate product safety, claims, and efficacy ▪ Undergo a risk-based assessment by bodies responsible for regulatory clearance and/or approval when appropriate to evaluate patient access to products
9. **Make claims appropriate to clinical evaluation and regulatory status**	▪ Ensure that product claims are appropriate to clinical evidence, regulatory status, and marketing authorization ▪ Adhere to labeling and advertising regulations under appropriate authorities, including labels and written, printed, or graphic matter accompanying or associated with the product ▪ Make claims appropriate to the highest level of clinical evaluation and regulatory status on all marketing materials and external-facing product information
10. **Collect, analyze, and apply real world evidence and product performance data**	▪ Conduct ongoing analysis and application of real world outcomes and product performance data to ensure ongoing product safety, efficacy, quality, and improvement ▪ Collect and analyze real world behavior data to enrich and further refine the product for better engagement, implementation, adherence, and user experience ▪ Design post-launch quality improvement initiatives for product use ▪ Employ a proactive approach to ongoing surveillance, assessment of user needs, and continuous learning