Table 1: Leveraging V3 for Digitally Derived Endpoints Framework - V3 as Applied to DHTTs Used in Various Drug Development Scenarios

KEY		
	The respective V3 assessment supporting prior clearance/approval of the DHTT in question is likely to provide much or all of the information needed	Prior V3 work should be assessed and leveraged if possible; additional work will likely be required, which may build on prior work
	There is no prior V3 work assessed by FDA for this scenario; new work will be needed for this step	

Scenario	Case Example	Verification	Analytical Validation	Clinical Validation	
		Is the tool accurate, precise, consistent across time, and uniform across different environmental bench testing conditions?	*Does the tool/algorithm accurately, reliably, and precisely generate the intended technical output from the input data, compared to the appropriate reference standard? Is the data flow defined and validated?*	*Is clinical validation required for the clinical outcome assessment or biomarker (e.g., monitoring, prognostic, predictive)?*	*Can the intent-to-treat population of the clinical trial use the tool? What is the patient burden? Are human factor studies needed?*
use of a cleared/approved digital health technology tool to measure a validated biomarker/COA/endpoint for a previously established concept of interest	PKG watch for PD tremor	since the digital health technology tool is cleared/approved, the verification assessment supporting prior clearance/approval of the DHTT is likely to provide much or all of the information needed	since the digital health technology tool is being used within its approved intended use, the analytical validation assessment supporting prior clearance/approval of the DHTT is likely to provide much or all of the information needed	since the approved intended use matches context of use, the clinical validation assessment supporting the prior clearance/approval of the DHTT is likely to provide much or all of the information needed	since the approved intended use covers the intent-to-treat population of the clinical trial, the clinical validation assessment supporting prior clearance/approval of the DHTT is likely to provide much or all of the information needed
use of a cleared/approval digital health technology tool to measure a validated biomarker/COA/endpoint for a new concept of interest	Actigraphy device with 510(k) clearance used by drug developer to assess bradykinesia/tremor in a study	since the digital health technology tool is cleared/approved, the verification assessment supporting the prior clearance/approval of the DHTT is likely to provide much or all of the information needed	since the digital health technology tool is being used outside of its approved intended use, analytical validation might need to be conducted- (e.g., new intent-to-treat population); prior work should be assessed and leveraged if possible; additional work will likely be required, which may build on prior work	Since the approved intended use may not match context of use, clinical validation needs to be confirmed; prior work should be assessed and leveraged if possible; additional work will likely be required, which may build on prior work	since digital health technology tool is being used outside its intended use, usability testing may be needed; prior work should be assessed and leveraged if possible; additional work will likely be required, which may build on prior work
use of a cleared/approved digital health technology tool to measure a previously established concept of interest used concept of interest to measure a novel biomarker/COA/endpoint	A wearable for a neuromuscular disease that is measuring walking distance (previously established endpoint) which records movement during daily living with high accuracy and precision. Only to be used within the study, not to be marketed in a post-market setting	since the digital health technology tool is cleared/approved, the verification assessment supporting the prior clearance/approval of the DHTT is likely to provide much or all of the information needed	since a cleared digital health technology tool is being used within its approved intended use, the analytical validation assessment supporting prior clearance/approval of the DHTT is likely to provide much or all of the information needed	need to confirm the context of use matches the approved intended us; prior work should be assessed and leveraged if possible; additional work will likely be required, which may build on prior work	since approved intended use covers the intent-to-treat population of the clinical trial, the analytical validation assessment supporting prior clearance/approval of the DHTT is likely to provide much or all of the information needed
use a cleared/approved digital health technology tool to measure a novel biomarker/COA/endpoint for a new concept of interest	Wearable with accelerometer/gyroscope (previously cleared for assessing sit-to-stand in muscular dystrophy) used in a study for assess sit-to-stand in Parkinson's disease.	since the digital health technology tool is cleared/approved, the verification assessment supporting the prior clearance/approval of the DHTT is likely to provide much or all of the information needed	since the digital health technology tool is being used outside of its approved intended use, analytical validation might need to be reconfirmed (e.g., new intent-to-treat population); prior work should be assessed and leveraged if possible; additional work will likely be required, which may build on prior work	since the approved intended use may not match context of use, clinical validation needs to be confirmed; prior work should be assessed and leveraged if possible; additional work will likely be required, which may build on prior work	since the digital health technology tool is being used outside its intended use, usability testing may be needed; prior work should be assessed and leveraged if possible; additional work will likely be required, which may build on prior work
use of a new digital health technology tool to measure a validated biomarker/COA/endpoint	Measure SV95C for DMD using a digital health technology tool	since the digital tool has not been cleared/approved, there is no prior V3 work assessed by FDA for this scenario; new work will be needed for this step	Since the digital tool has not been cleared/approved, there is no prior V3 work assessed by FDA for this scenario; new work will be needed for this step	need to confirm the context of use in the clinical setting matches the validated endpoint; prior work should be assessed and leveraged if possible; additional work will likely be required, which may build on prior work	since the digital tool has not been cleared/approved, there is no prior V3 work assessed by FDA for this scenario; new work will be needed for this step
use of new digital health technology tool to measure a novel biomarker/COA/ endpoint	Sensor-based measures collected by mobile application (app; smartphone and wrist-worn wearable) to assess change in baseline for a progressive neurodegenerative disease through both active and passive tests	since the digital tool has not been cleared/approved, there is no prior V3 work assessed by FDA for this scenario; new work will be needed for this step	since the digital tool has not been cleared/approved, there is no prior V3 work assessed by FDA for this scenario; new work will be needed for this step	must define context of use, and, as there is no prior V3 work assessed by FDA for this scenario; new work will be needed for this step	Since the digital tool has not been cleared/approved, there is no prior V3 work assessed by FDA for this scenario; new work will be needed for this step