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Regenerative Medicine Resource Center

MEDICAL DEVICE TRANSLATIONAL DEVELOPMENT STATUS QUESTIONNAIRE

item #	Translational Development Phase 1: RESEARCH & PLANNING	STATUS?	Translational Development Phase 2: PRECLINICAL DEVELOPMENT: FEASIBILITY	STATUS?	Translational Development Phase 3: PRECLINICAL DEVELOPMENT: VERIFICATION	STATUS?	Translational Development Phase 4: PRECLINICAL DEVELOPMENT:GLP VALIDATION	STATUS?	Translational Development Phase 5: CLINICAL DEVELOPMENT:IDE PREPARATION	STATUS?
1	**Clinical Need & Market Assessment** • Preliminary clinical user needs • Preliminary intended use statement (including users: clinician, patient, care giver, etc.) • Preliminary market analysis/ requirements		**Initial Prototype Design** • Development plan & project schedule • Preliminary design input requirements (including clinical user needs, human factors, and IP plans) • Preliminary Hazard Analysis (PHA)/ Risk Management Plan (RMP) • Materials/ functional specifications: includes biocompatibility, sterilization, packaging/ shelf life, labeling specs		**Device Design Verification** • Update development plans & schedule (including commercialization and marketing plans) • Update Preliminary Hazard Analysis (PHA)/ Risk Management Plan (RMP) • Revise Device Master Record (DMR) drawings • Prepare/ approve design verification plan • Prepare/ approve verification protocols, including materials biocompatibility & preliminary sterilization		**Device GLP Performance Validation** • Prepare/ approve GLP validation plan • Ensure optimal animal model, statistics, etc. • Finalize GLP supplier agreement • Prepare/ approve GLP validation protocols, with clinical user input		**IDE Clinical Performance Validation** • Prepare/ approve clinical validation plan • Clarify NSR or SR Study Requirements • NSR Study Protocol to be IRB approved • SR Study Protocol to be FDA & IRB approved • Determine need for pre-IDE meeting w/ FDA • Select & qualify clinical study sites	
2	**Preliminary Regulatory Pathway** • Preliminary regulatory basis assessment • FDA Regulation Number & Code FDA Device Class [I, II, III / 510(k) / PMA] • IDE Required: Non-Significant Risk (NSR) Study or Significant Risk (SR) Study • Combination Product? Will Request for Designation (RFD) be needed?		**Prototype Design Confirmation** • Preliminary product specifications accepted • Initial prototype builds • Initial prototype confidence testing • Initial acceptance criteria met • Revise draft engineering drawings		**Initial Builds for Verification** • Prepare initial manufacturing work instructions • Build verification test units • Conduct design verification protocols, including biocompatibility and sterilization method • Prepare/ approve design verification reports		**Pilot GMP Production** • Build pilot GLP devices per DMR • Quality Assurance (QA) Inspection of pilot GLP devices • Document production equivalence • Compile GLP device history record		**Pre-IDE Meeting w/ FDA (for SR Study)** • Schedule pre-IDE meeting w/ FDA • Prepare draft IDE clinical protocol/ informed consent (IFC), with clinical user input • Prepare/ submit pre-IDE to FDA • Record formal pre-IDE minutes & update clinical validation plan based on FDA inputs from pre-IDE meeting	
3	**Financial Considerations** • Initial sources of funding support identified • Potential follow-on funding sources identified		**Quality Planning** • Establish Quality System SOPs • Document reviews & change controls • Develop Protocol/Experiment Requirements Document (ERD) • Supplier qualifications & controls • Preliminary manufacturability assessment		**Device Design Acceptability** • Confirm Design Outputs meet Design Input requirements • Update DIDO Matrix • Prepare device performance specification • Update Design History File (DHF)		**GLP Validation Testing** • GLP testing protocol outline • Conduct approved GLP protocol(s) • Prepare/ approve GLP validation report(s) • Do GLP validation results confirm Intended Use & Meet User Needs?		**IDE Clinical Study Approval** For NSR Clinical Study: • Finalize NSR clinical study protocol, with clinical user input • Submit protocol/ IFC for IRB approval • Receive written IRB approval For SR Clinical Study: • Prepare/ submit IDE to FDA for review/ approval • 30-day FDA IDE review clock begins • Respond to FDA IDE request/ questions • Receive written IDE approval from FDA	
4	**Preliminary Intellectual Property (IP) Assessment** • Provisional patent application filed • USA • PCT/Foreign		**Initiate Design History File (DHF)** • Revise Design Input & planning documents • Update project schedule • Draft Design Input/ Design Output (DIDO) Trace Matrix • Draft Device Master Record (DMR)		**Revise Device Design Documentation** • Update specifications, drawings, manufacturing work instructions (i.e., DMR) based on verification results • Update DIDO Matrix • Approve device performance specification		**Preclinical Design Changes** • Determine need for design changes based GLP validation report results • Update DIDO Matrix, RMP, Device Performance Spec & Related DHF Docs		**IDE Clinical Study Start-Up Prep** • Finalize clinical study funding resources • Finalize clinical study site agreements • Finalize clinical study documents based on IRB/ FDA review/ approvals • Finalize clinical study data capture tools (paper based or electronic data capture (EDC))	
5	**Preliminary Proof of Concept** • Preliminary scientific questions addressed • Product concept document acceptable **GO / NO GO to move to PHASE 2** • Identify ITP follow-on funding + budget/ industry partnerships		**Prototype Design Review** • Review product specifications and approve • Review DHF documents • Record design review minutes/ results **GO / NO GO to move to PHASE 3** • Identify ITP follow-on funding + budget/ industry partnerships		**Design Acceptability Review** • Do all Design Outputs meet Design Input requirements to Move to GLP Performance Validation Testing? • Approve design acceptability decision **GO / NO GO to move to PHASE 4** • Identify ITP follow-on funding + budget/ industry partnerships		**Preclinical Design Freeze** • Conduct GLP Device Design Review • Confirm GLP Device Design, Intended Use & User Needs have been met • Record design review minutes/ results **GO / NO GO to move to PHASE 5** • Identify ITP follow-on funding + budget/ industry partners		**ITP Project Close-Out** • Identify ITP follow-on funding + budget/ industry partnerships • Compile device DHF/ DMR related records • Prepare ITP final report **CELEBRATE, Then Prepare 510(k) or PMA For FDA Submittal**	

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DRUG* TRANSLATIONAL DEVELOPMENT STATUS QUESTIONNAIRE

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1	**Clinical Need & Market Assessment** • Preliminary clinical user needs • Preliminary intended use statement (including users: clinician, patient, care giver, etc.) • Preliminary market analysis/ requirements		**Initial API Feasibility** • Preclinical development plan & project schedule • Preliminary target API specifications drafted, including stability • API source manufacturer identified • API source manufacturer qualified		**Non-Clinical Drug Manufacturing & Evaluation** • Update development plans & schedule • Select non-clinical drug testing supplier • Qualify manufacturer • Manufacture drug for non-clinical testing		**GLP Drug Testing To Enable IND** • Update development plans & schedule • Engage GMP drug manufacturer • Quality Assurance (QA) audit/ qualify GLP drug testing supplier • Finalize GMP/ GLP supplier agreements		**IND Clinical Study Preparation** • Prepare/ approve clinical validation plan • Draft Phase 1 clinical protocol summary • Select & qualify clinical study PI/ sites	

2	**Preliminary Regulatory Pathway**
	• Preliminary regulatory basis assessment
	• Product regulated as:
	  ○ Drug
	  ○ Biologic
	  ○ Human Cellular / Tissue
	  ○ Combination Product – RFD Needed
			API Formulation / Development
			• Establish API specifications (formulation)
			• Confirm drug manufacturing supplier
			• Draft SOPs for drug manufacturing
			• Drug manufacturing process verified
					Non-Clinical Drug Testing
					• Prepare/ approve non-clinical drug safety protocols
					• Prepare/ approve non-clinical drug effectiveness protocols
							GLP Drug Testing Prep (Validation)
							• GLP testing protocol outline
							• Prepare GMP drugs for GLP studies
							• Prepare/ approve (IACUC) GLP protocols to assess toxicology/ Absorption, Distribution, Metabolism, Excretion (ADME)/ Safety & Effectiveness (S&E)/ Stability
									Pre-IND Meeting w/ FDA
									• Schedule pre-IND meeting w/ FDA
									• Prepare draft IND clinical protocol/ informed consent (IFC), with clinical user input
									• Prepare/ submit pre-IND to FDA
									• Record formal pre-IND minutes
									• Revise clinical protocol based on FDA inputs from pre-IDE mtg	

3	**Financial Considerations** • Initial sources of funding support identified • Potential follow-on funding sources identified • Preliminary exit strategy objectives identified		**Quality Planning** • Establish relevant quality SOPs • Document reviews & change controls • Develop Protocol/Experiment Requirements Document (ERD) • Supplier qualifications & controls • Preliminary QA/ manufacturability/ supplier assessment		**Preliminary Drug Acceptability** • Prepare/ approve non-clinical drug safety test reports • Prepare/ approve non-clinical drug effectiveness test reports		**Pivotal GLP Drug Testing** • Prepare GLP protocol with clinical user input • Conduct approved GLP protocol(s) • Prepare/ approve GLP study report(s)		**IND Submission** • Prepare/ submit IND to FDA for review/ approval • 30 day FDA IND review clock begins • Respond to FDA IND questions	
4	**Preliminary Intellectual Property (IP) Assessment** • Provisional patent application filed • USA • PCT/Foreign		**Preliminary Non-Clinical Drug Safety** • Pharmacokinetics (PK) & Pharmacodynamics (PD) • Preliminary toxicology (Tox)		**Refine Drug Formulation** • Update drug specs, formulation based on test report results, as needed		**Pivotal GLP Drug Acceptability Assessment** • Update drug specifications, formulation based on GLP results • Do GLP study results confirm preliminary Safety & Effectiveness (S&E) to allow first-in-human (FIH) clinical trial • Ready to initiate GMP scale-up for IND		**IND Clinical Study Start-Up Prep** • Finalize clinical study funding resources • Finalize clinical study site agreements • Finalize clinical study docs based on IRB/ FDA review/ approvals • Finalize clinical study data capture tools (paper based or electronic data capture (EDC))	
5	**Preliminary Proof of Principal** • Target Active Pharmaceutical Ingredient (API) identified • Target patient population identified • Preliminary scientific questions addressed **GO / NO GO to move to PHASE 2** • Identify ITP follow-on funding + budget/ industry partnerships		**Drug Feasibility Review** • Review drug product (i.e., formulated API), preliminary PK, PD, & Toxicology • Confirm preliminary QA/ manufacturing supplier • Record feasibility review minutes/ results **GO / NO GO to move to PHASE 3** • Identify ITP follow-on funding + budget/ industry partnerships		**Preliminary Drug Acceptability Review** • Is the drug reasonably safe to move to GLP studies? • Approve drug acceptability decision **GO / NO GO to move to PHASE 4** • Identify ITP follow-on funding + budget/ industry partnerships		**Is Investigational Drug Ready Enable IND** • Record investigational drug acceptability decision minutes/ results **GO / NO GO to move to PHASE 5** • Identify ITP follow-on funding + budget/ industry partnerships		**ITP Project Close-Out** • Identify ITP follow-on funding + budget/ industry partnerships • Compile drug development related records • Prepare ITP final report **CELEBRATE, Then Prepare NDA For FDA Submittal**	

*** A Similar Translational Development Approach Is Taken For Biological Products Under 21 CFR §600, 21 CFR §601 & 21 CFR §610.**

Translating Dental, Oral, and Craniofacial Regenerative Medicine Innovations to the Clinic through Interdisciplinary Commercial Translation Architecture. Taylor et al. JDentRes 2021