CMC DEVELOPMENT PLAN IN PLACE (CP-ADDS)LG

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

A detailed plan for completing the definition and planning of the combination product FIH stage gate.

CMC development plan updated.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF - DETAIL NEEDED AT EACH GATE
▪ List of activities that will be conducted, that lead to achieving Product Definition and Planning milestone at FIH stage gate	Plans to complete the following bolded items by the next stage gate: • User capabilities and preferences assessment • Ethnographic studies completion • Hazard identification initiation • Concept assessment completion • **Design and development plan initiation** • **Instructions for Use drafts** • **Human Factors Study Plan** • **Application risk assessment completion** • **Design History File initiation** • **Design Input Review completion** • **High-level Project Plan and definition of critical product attributes (if prototype available)** • **Preliminary device prototype generation** • Design Output Review completion • Formative human factors study completion • Design risk assessment completion • Process risk assessment completion • Critical component dimensions and specifications definition • Design and Development Plan updates • Instructions for Use updates • Design History File updates • Engineering testing of prototype and conduct simulated use or clinical testing • Summative human factors study initiated • Design verification execution • Design Verification Review completion • Design validation execution • Design Validation Review completion • Design transfer completion • Design Transfer Review completion • Supply chain / logistics plan completion • Complaint handling process definition • Pharmacovigilance plan completion Completed in PCD stage	▪ A detailed plan to achieve the FIH CMC milestones is expected ▪ Additionally, the plan should identify potential development risks to launch and risk mitigation strategies related to development timeline, costs, and resource allocation

* Items in **bold** font reflect suggested reporting guidelines for this stage gate

CMC DEVELOPMENT PLAN IN PLACE (DRUGS)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

A Detailed plan to complete initial substance (DS) and drug product (DP) characterization, and define the initial cGMP manufacturing process.

CMC development plan initiated.

(The CMC Development Plan is initiated during discovery and preclinical development and is expected to be in place by the PCD stage gate)

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ List of activities that will be conducted, that lead to achieving the "Initial DS/DP Characterization" milestone at FIH stage gate	• **Complete initial drug product characterization** • **Define cGMP manufacturing process** • **Complete GMP manufacturing for Ph 1** • Finalize DS characterization & analytical method development • Manufacture DS at kilo-scale • Complete DP characterization • Complete DP package characterization • Manufacture DP to support the Phase 2 clinical trial • Manufacturing process optimization • GMP manufacturing for Ph 3 • Readiness for Tech Transfer • Technology transfer and validation of raw material, drug substance, and drug product analytical and functional release testing • Technology transfer and validation of drug substance & drug product manufacturing and packaging processes • Qualification of commercial-scale facilities • Commercial launch strategy • QA/compliance activities • Ongoing CMC Support to ensure uninterrupted supply of high quality DP in all markets	▪ A detailed plan to achieve the FIH CMC milestones is expected ▪ Additionally, the Plan should identify potential development risks to PQ, and risk mitigation strategies related to development timeline, costs and resource allocation

* Items in **bold** font reflect suggested reporting guidelines for this stage gate

CMOs-CROs SELECTED (1/2)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Rationale and justification for selection of drug development partners.

Drug development service providers engaged and qualified
(*Partner Selection may be completed prior to either the PCD or FIH gate reviews, depending on specific product requirements)

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Contract research partners (to facilitate / enable preclinical process development) engaged and qualified	a) Scope of work required (e.g., functional activities, process & method development, etc.) b) Partner engagement strategy (e.g., outsourced activity, insourced activity, consultation, etc.) c) cGLP certification d) Audits by FDA / NRAs and client e) Confirmation of capabilities, equipment, equipment qualification & process/method validation packages, staff training, SOPs, etc. f) Previous experience with partner (e.g., successes & failures) g) Preliminary cost information h) Lead times / time in the queue i) Contract terms and long-term contingencies	▪ Summary of key data and rationale to support partner selection ▪ Additional detail may be reported in an appendix

CMOs-CROs SELECTED (2/2)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Rationale and justification for selection of drug development partners.

Drug development service providers engaged and qualified
(*Partner Selection may be completed prior to either the PCD or FIH gate reviews, depending on specific product requirements)

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Contract manufacturing partners (to facilitate / enable clinical supply) engaged and qualified *** CMC experts should be engaged to assess partners for drug substance, drug product manufacturing and analytical services**	a) Scope of work required (e.g., functional activities, process & method development, etc.) b) Partner engagement strategy (e.g., outsourced activity, insourced activity, consultation, etc.) c) cGMP certification d) Audits by FDA / NRAs and client e) Confirmation of capabilities, capacity, quality control systems, equipment, equipment qualification & process/method validation packages, staff training, SOPs, etc. f) Previous experience with partner (e.g., successes & failures) g) Preliminary cost information h) Lead times / time in the queue i) Contract terms and long-term contingencies	▪ Summary of key data and rationale to support partner selection ▪ Additional detail may be reported in an appendix
▪ Support service partners (e.g., to enable initial regulatory requirements, file patents, provide legal counsel, etc.) engaged and qualified	a) Scope of work required (e.g., IND preparation, patent creation, legal counsel, etc.) b) Partner engagement strategy (e.g., outsourced activity, insourced activity, consultation, etc.) c) Confirmation of capabilities & services d) Previous experience with partner (e.g., successes & failures) e) Preliminary cost information f) Lead times / time in the queue	▪ Summary of key data and rationale to support partner selection ▪ Additional detail may be reported in an appendix

CONCEPT SCREENING AND IDENTIFICATION

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

To define and select device concept(s) for drug-device combination product candidate with viable capability to meet the TPP

Concept(s) generated based on based on initial market and user needs and TPP.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Hazard identification initiated	a) Use related hazard analysis and assessment, either by application of analytical techniques or by user-based evaluations b) Evaluation of prototype (if prototype is available) c) Potential risk mitigation strategies that may be employed given the product concept and application	▪ Summary of key data / information or information to substantiate conclusions ▪ Illustrative data tables or figures may be reported in an appendix
▪ Concept assessed	a) Evaluation of whether TPP goals can be achieved with an already approved device. If not, definition of the product concept(s) and "proof" that this product, as defined, can be developed and manufactured (based on early testing and existing product data) b) High level assessment of manufacturing capability (changes/new) needed and data suggesting that COGS target can be met c) Anticipated technical risks (high level) and how CMC Development plan for FIH stage gate addresses these risks	

*Candidate progression is discussed at standing grantee update meetings with the investment team

LEAD CHEMICAL SERIES SELECTED

GLOBAL DRUG DEVELOPMENT

Goals/Definition

Selection of lead series that meet criteria for progression to Lead Optimization.
Drug target validated and lead identified for optimization.**

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Screening Strategy Established and Target validated (if possible)	a) Mechanism of action & target validation (e.g., biomarkers, assays, *in vitro* / *in vivo* assessments, etc.)** b) Lead identification strategy defined • Lead identification screening process (e.g., compound library, HTS, computer-based design, combinatorial chemistry, assays, phenotypic *in vitro* / *in vivo* assessments, etc.) • Selection criteria for 'actives' • Screening cascade strategy	▪ Summary of key data to substantiate conclusions ▪ Illustrative data tables or figures may be reported in an appendix
▪ Lead identification *** CMC experts should be engaged to assess physicochemical properties**	a) Screening assays (developed and validated) b) Profile hits (e.g., binding affinity, dose-response, specificity, assays, *in vitro* assessments, etc.) c) Structure-activity relationships d) Assessment of physicochemical properties* e) For phenotypic hits, mechanism of action defined if feasible f) Off-target profiling (e.g., secondary pharmacology, hERG, cytotoxicity, etc.) g) Assessment of reactive metabolite liability h) Drug-drug interaction considerations i) Lead optimization strategy defined	▪ Summary of key data to substantiate conclusions ▪ Illustrative data tables or figures may be reported in an appendix

**** It is understood that not all programs will be able to validate the target at this stage in the process**

LEAD OPTIMIZATION COMPLETED (1/2)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

To evaluate basic pharmaceutical properties such as solubility, stability, and physical state of multitude of chemical modifications of the lead scaffold.

Lead optimization completed and candidate for preclinical candidate development selected.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Lead candidate optimized	a) *In vitro*, *in silico* & *in vivo* (animal) model development and dose response relationships established. b) Preliminary *in vitro* / *in vivo* safety / toxicology & *in vivo* efficacy (e.g., safety pharmacology, acute toxicology, genotoxicity, cytotoxicity, reactive metabolite formation) c) PK and ADME properties optimized and modeling indicates likely to achieve TPP PK goals in human. d) PK-PD relationship established using animal model of disease state (preferred) or alternate functional assay e) Biomarker ID in place for target engagement f) Off-target screening in place and selectivity achieved g) Initial pharmaceutical considerations (e.g. stability, solubility, synthetic feasibility, formulation strategy, etc.) h) Preclinical candidate selection justification package	▪ Summary of key data to substantiate conclusions ▪ Illustrative data tables or figures may be reported in an appendix
▪ Drug combination assessment	a) Need for combination considerations b) Assessment strategy	▪ One page summary
▪ Candidate molecule meets target product profile	a) Alignment with Foundation (intervention) target product profile b) Feasibility and benefit over existing treatments	▪ The cTPP and iTPP may be compared side by side in a table format

***Candidate progression is discussed at standing grantee update meetings with the investment team**

LEAD OPTIMIZATION COMPLETED (2/2)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

To evaluate basic pharmaceutical properties such as solubility, stability, and physical state of multitude of chemical modifications of the lead scaffold.

Initial drug substance characterization completed and preclinical formulation developed.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Initial drug substance characterization completed *** CMC experts should be engaged to assess physicochemical properties**	a) Molecular & physicochemical properties (e.g., chirality /enantiomer inter-conversion, solubility (pKa, Log P/Log D), permeability (Caco-2 permeability coefficient), BCS classification, etc.) b) Thermal analysis, DSC c) Salt & form screening (e.g., amorphous vs. crystalline, polymorph ID, etc.) d) Drug substance / preliminary drug product stability studies (e.g. solid state drug substance stability, metabolic stability) e) Chemical purity (e.g., impurity identification & profiles, analytical methods) f) Stability studies (e.g., T, pH, humidity, light, metabolic stability, etc.) g) Stable, bioavailable salt/form selected	▪ Summary of key data to substantiate conclusions ▪ Illustrative data tables or figures may be reported in an appendix
▪ Preclinical formulation to support animal studies completed	a) Preliminary drug substance formulation (e.g., salt/form analysis, polymorph characterization, delivery method, confirm bioavailability / PK in animal) b) Formulation considerations related to type of animal studies (e.g. Biomarkers / Preclinical PoC, PKDM and tox studies) and route of administration (e.g. oral / IP / IV / SC) c) Drug substance characterization and formulation for active comparators (known compounds, benchmarks etc.) d) GLP analytical methods for formulation stability and release e) Particle size / oral bioavailability, need for milling / micronization	▪ Summary of key data to substantiate conclusions ▪ Illustrative data tables or figures may be reported in an appendix

***Candidate progression is discussed at standing grantee update meetings with the investment team**

USER NEEDS AND ACCEPTANCE

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Develop a set of user needs that can be ultimately translated into device requirements.

User needs capture what the device does or should do and acceptability of those needs across different geographies.

CRITERIA	SAMPLE CONTENT REQUIREMENT
▪ Intended use, User capabilities and preferences assessed ▪ Ethnographic studies and user needs conducted	a) Assessment of use case, user needs, capabilities, and acceptance (user needs often cannot be finalized before TPP creation) developed within delivery workstream b) Assessment of market and healthcare ecosystem (procurer requirements (incl. costing considerations), provider, governmental support, etc.) developed within delivery workstream c) Ethnographic studies to evaluate the care setting, cultural factors, and other factors associated with intended application and setting d) Task analysis as a precursor to human factors engineering

BUSINESS CASE UPDATED

GLOBAL DRUG DEVELOPMENT

Goals/Definitions

Business case for developing a deliverable product

Business Case, deliverability assessment, strategic demand forecast and COGS reports and cost effectiveness report

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE

▪ Business Case	• Business case provides overview of product candidate's strategic value and market viability, including:
	  • Value proposition against foundation's disease strategy and other interventions in market
	  • Estimate of overall costs to launch and drive uptake
	  • Summary of market understanding (e.g., size, segments, user needs, etc.)
		▪ Provide key assumptions and rationale for business case

CLINICAL DEVELOPMENT PLAN UPDATED

GLOBAL DRUG DEVELOPMENT

Goals / Definition
Clinical safety data and rationale for Phase 2 dose selection.

Clinical Development Plan initiated.
(*Clinical Development Plan is initiated prior to the FIH gate review and is updated & reviewed during development through to the DTF gate review.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Clinical development plan updated	a) Overview of planned clinical activities: • Study phase, objectives / research rationale • Duration of the studies, number of subjects, recruitment criteria (e.g.,. study arms, patient cohorts, comparators for non-inferiority trials, power calculations etc.) • Dosing & dosing modeling strategies • Detailed rationale for Phase 2 dose range, and target clinical exposures • Toxicology and toxicokinetic results to support doses and dosing duration in Phase 2 • Drug combination assessment & plan • Toxicology plan to support Phase 3 b) Clinical partners, proposed target countries, and study sites (based on criteria including clinical expertise, sustainability, site capacity, and disease incidence / epidemiology studies, etc.) c) Definition of clinical endpoints (primary & secondary), methodology (clinical endpoint assays, data collection plan, statistical methods, etc.), adverse event reporting, stopping rules, etc. d) Monitoring, data management, and biostatistics strategies e) Post-marketed product surveillance / Phase 4 trial strategy f) Mass product administration considerations (e.g., trial design, safety requirements, etc.) g) Off-label use considerations h) Trial size considerations for diseases with limited incidence rates i) Potential risks and mitigation strategies j) Timelines and budgets for clinical development	▪ Detailed Phase 2 clinical plan with timeline including supporting CMC and tox plans ▪ High-level / draft plan for Phase 3 ▪ Updated risk identification and mitigation needed for all subsequent phases of development ▪ Plans should reflect approaches to accelerate decision making (e.g., adaptive designs, real-time data analysis of clinical trials etc.) ▪ Phase 2 plan is modified during Phase 1 trial as Phase 1 data become available ▪ Clinical development plan extends beyond DTF to accommodate the time needed to report Phase 3 results and also cover additional plans for pediatric studies and post-market surveillance

CMC DEVELOPMENT PLAN UPDATE (CP/ADDS) (1/2)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

A detailed plan for completing design verification and validation of the combination product at EP2 stage gate.

CMC development plan updated.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ List of activities that will be conducted, that lead to achieving Product Definition and Planning milestone at EP2 stage gate	Plans to complete the following bolded items by the next stage gate: • User capabilities and preferences assessment • Ethnographic studies completion • Hazard identification initiation • Concept assessment completion • Design and development plan initiation • Instructions for Use drafts • Human Factors Study Plan • Application risk assessment completion • Design History File initiation • Design Input Review completion • High-level Project Plan and definition of critical product attributes (if prototype available) • Preliminary device prototype generation • Design Output Review completion • Formative human factors study completion • Design risk assessment completion • Process risk assessment initiated • Critical component dimensions and specifications definition • Design and Development Plan updates • Instructions for Use updates • Design History File updates • Engineering testing of prototype and conduct simulated use or clinical testing • **Summative human factors study initiated** • **Design verification execution** • **Design Verification Review completion** • **Design validation execution** • **Design Validation Review completion** • Design transfer completion • Design Transfer Review completion • Supply chain / logistics plan completion • Complaint handling process definition • Pharmacovigilance plan completion	▪ A detailed plan to achieve the FIH CMC milestones is expected ▪ Additionally, the plan should identify potential development risks to launch and risk mitigation strategies related to development timeline, costs, and resource allocation

* Items in **bold** font reflect suggested reporting guidelines for this stage gate

CMC DEVELOPMENT PLAN UPDATE (CP/ADDS) (2/2)

GLOBAL DRUG DEVELOPMENT

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
• Process risk assessment initiated	a) Critical molding and assembly process parameters b) Identification of CMOs and assessment of impact on manufacturing costs and COGS c) Creation of manufacturing flow diagram and assess product demand to verify COGS based on projected demand forecast	a) Summary report containing key data / information to substantiate conclusions b) Illustrative data tables or figures may be reported in an appendix
• Critical component dimensions and specifications defined	a) Initiation of stability studies development b) Initiation of development packaging and labeling processes c) Transportation studies to determine if there are potential interactions between drug and device during transportation that would impact the performance/efficacy of the functioning of the device as well as the safety and efficacy of the drug action d) Verification and Validation Plans	
• Instructions for Use updated	a) Updated Instructions for Use as data/information becomes available at the appropriate points in the development stage	a) Summary report containing key data / information to substantiate conclusions b) Illustrative data tables or figures may be reported in an appendix
• Engineering testing of prototype and conduct simulated use or clinical testing	a) Completion of prototype for Summative Human Factors Studies	

* Items in **bold** font reflect suggested reporting guidelines for this stage gate

CMC DEVELOPMENT PLAN UPDATED (DRUGS)

GLOBAL DRUG DEVELOPMENT

Goals / Definition

To describe a detailed plan to complete process optimization considering feasibility for full-scale manufacturing, including a plan to assess tech transfer readiness to commercial scale manufacturing.

cGMP DS manufactured at kilo-scale and scale-up processes defined.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ List of activities that will be conducted, that lead to achieving the "Full-Scale DS/DP Manufacturing Process Optimized" and "Tech Transfer and Validation Plan In Place" milestones at EP2 stage gate	• Complete initial drug product characterization • Define cGMP manufacturing process • Complete GMP manufacturing for Ph 1 • Finalize DS characterization & analytical method development • Manufacture DS at kilo-scale • Complete DP characterization • Complete DP package characterization • Manufacture DP to support the Phase 2 clinical trial • **Manufacturing process optimization** • **GMP manufacturing for Ph 3** • **Readiness for Tech Transfer** • **Technology transfer and validation of raw material, drug substance, and drug product analytical and functional release testing** • **Technology transfer and validation of drug substance & drug product manufacturing and packaging processes** • **Qualification of commercial-scale facilities** • Commercial launch strategy • QA/compliance activities • Ongoing CMC Support to ensure uninterrupted supply of high quality DP in all markets	▪ A detailed CMC plan to achieve the EP2 CMC milestones is expected ▪ Additionally, the Plan should identify potential development risks to PQ, and risk mitigation strategies related to development timeline, costs and resource allocation

* Items in **bold** font reflect suggested reporting guidelines for this stage gate

COGS UPDATED

GLOBAL DRUG DEVELOPMENT

Goals/Definitions

Business case for developing a deliverable product

Business Case, deliverability assessment, strategic demand forecast and COGS reports completed

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE

▪ COGS	• An initial, high-level COGS analysis at EP1 will identify:
	  • Key cost drivers
	  • Cost estimate assumptions for equipment needed, processes
	  • Projected price (within 30% of TPP target)
		▪ BMGF provides methodology

COST-EFFECTIVENESS ANALYSIS UPDATED

GLOBAL DRUG DEVELOPMENT

Goals/Definitions

Business case for developing a deliverable product

Business Case, deliverability assessment, strategic demand forecast and COGS reports completed

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE

▪ Cost-Effectiveness Analysis	• An initial, high-level cost-effectiveness analysis will identify:
	  • Anticipated health and economic benefits of the product
	  • Projected health and economic costs to achieve the benefits
	  • Comparisons to existing standards of care
		▪ BMGF provides methodology

DELIVERABLITY ASSESSMENT UPDATED

GLOBAL DRUG DEVELOPMENT

Goals/Definitions

Business case for developing a deliverable product

Business Case, deliverability assessment, strategic demand forecast and COGS reports and cost effectiveness report

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Deliverability Assessment	• A deliverability assessment will provide a high-level assessment of risks and opportunities for: • Improvement relative to standard of care • Considerations around the global and country awareness of the intervention, possibility of financing, • Global policy and regulatory pathway • Supply chain and user targeting • Frequency and mode of delivery and any special handling required • Novelty relative to existing products • Manufacturing considerations • Provider-related issues including workflow and training (ex: maintenance and calibration) • Patient access, perception of value and economics • Disease risk awareness in population	▪ Summary report

DELIVERY MILESTONES FOR DECISION TO ENTER PHASE 2 TRIALS (1/2)

GLOBAL DRUG DEVELOPMENT

Goals/ Definitions

Business case for developing a deliverable product.

Business Case, deliverability assessment, strategic demand forecast and COGS reports and cost effectiveness report.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE

▪ Business Case	• Business case provides overview of product candidate's strategic value and market viability, including:
	  • Value proposition against foundation's disease strategy and other interventions in market
	  • Estimate of overall costs to launch and drive uptake
	  • Summary of market understanding (e.g., size, segments, user needs, etc.)
		▪ Provide key assumptions and rationale for business case

▪ Deliverability Assessment	• A deliverability assessment will provide a high-level assessment of risks and opportunities for:
	  • Improvement relative to standard of care
	  • Considerations around the global and country awareness of the intervention, possibility of financing,
	  • Global policy and regulatory pathway
	  • Supply chain and user targeting
	  • Frequency and mode of delivery and any special handling required
	  • Novelty relative to existing products
	  • Manufacturing considerations
	  • Provider-related issues including workflow and training (ex: maintenance and calibration)
	  • Patient access, perception of value and economics
	  • Disease risk awareness in population
		▪ Summary report

DELIVERY MILESTONES FOR DECISION TO ENTER PHASE 2 TRIALS (2/2)

GLOBAL DRUG DEVELOPMENT

Goals/ Definitions

Business case for developing a deliverable product.

Business Case, deliverability assessment, strategic demand forecast and COGS reports and cost effectiveness report.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE

▪ Strategic Demand Forecast	• An initial, high-level demand forecast will identify:
	  • Target countries
	  • Target sub populations
	  • Timing of introduction specific to identified countries
		▪ BMGF provides methodology

▪ COGS	• An initial, high-level COGS analysis at EP1 will identify:
	  • Key cost drivers
	  • Cost estimate assumptions for equipment needed, processes
	  • Projected price (within 30% of TPP target)
		▪ BMGF provides methodology

▪ Cost-Effectiveness Analysis	• An initial, high-level cost-effectiveness analysis will identify:
	  • Anticipated health and economic benefits of the product
	  • Projected health and economic costs to achieve the benefits
	  • Comparisons to existing standards of care
		▪ BMGF provides methodology

DELIVERY MILESTONES FOR DECISION TO ENTER PHASE 2 TRIALS (1/2)

GLOBAL DRUG DEVELOPMENT

Goals/ Definitions

Business case for developing a deliverable product.

Business Case, deliverability assessment, strategic demand forecast and COGS reports and cost effectiveness report.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Business Case	• Business caseprovides overview of product candidate's strategic valueand market viability, including: • Value proposition against foundation's diseasestrategy and other interventions in market • Estimate of overall costs to launch and driveuptake • Summary of market understanding (e.g., size, segments, user needs, etc.)	▪ Providekey assumptions and rationale for business case
▪ Deliverability Assessment	• A deliverability assessment will providea high-level assessment of risks and opportunities for: • Improvement relativeto standard of care • Considerations around theglobal and country awareness of the intervention, possibility of financing, • Global policy and regulatory pathway • Supply chain and user targeting • Frequency and mode of delivery and any special handling required • Novelty relativeto existing products • Manufacturing considerations • Provider-related issues including workflow and training (ex: maintenance and calibration) • Patient access, perception of valueand economics • Disease risk awareness in population	▪ Summary report

DELIVERY MILESTONES FOR DECISION TO ENTER PHASE 2 TRIALS (2/2)

GLOBAL DRUG DEVELOPMENT

Goals/ Definitions

Business case for developing a deliverable product.

Business Case, deliverability assessment, strategic demand forecast and COGS reports and cost effectiveness report.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE

▪ Strategic Demand Forecast	• An initial, high-level demand forecast will identify:
	  • Target countries
	  • Target sub populations
	  • Timing of introduction specific to identified countries
		▪ BMGF provides methodology

▪ COGS	• An initial, high-level COGS analysis at EP1 will identify:
	  • Key cost drivers
	  • Cost estimate assumptions for equipment needed, processes
	  • Projected price (within 30% of TPP target)
		▪ BMGF provides methodology

▪ Cost-Effectiveness Analysis	• An initial, high-level cost-effectiveness analysis will identify:
	  • Anticipated health and economic benefits of the product
	  • Projected health and economic costs to achieve the benefits
	  • Comparisons to existing standards of care
		▪ BMGF provides methodology

DESIGN HISTORY FILE UPDATED

GLOBAL DRUG DEVELOPMENT

Goals/ Definitions

To update the compilation of documentation that describes the design history of a finished medical device.

The DHF contains or references the records necessary to demonstrate that the design was developed in accordance with the approved design plan.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
• Design History File updated	a) Updated Design History File as data/information becomes available at the appropriate points in the development stage b) Changes made to product need to be captured within the Design History File	

DESIGN OUTPUT REVIEW

GLOBAL DRUG DEVELOPMENT

Goals / Definitions

Conduct a Design Output Review which includes production specifications as well as descriptive materials which define and characterize the design.

Design review is a documented, comprehensive, systematic examination of a design to evaluate the adequacy of the design requirements, to evaluate the capability of the design to meet these requirements, and to identify problems.

In general, formal design reviews are intended to:

- **provide a systematic assessment of design results, including the device design and the associated designs for manufacturing (DFM) production and support processes;**
- **provide feedback to designers on existing or emerging problems;**
- **assess project progress; and/or**
- **provide confirmation that the project is ready to move on to the next stage of development.**

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
• Design Output Review conducted	a) Conclusions and recommendations from the Design Output Review b) Control plans updated based on risk assessment and Design Output Review	

DESIGN RISK ASSESSMENT

GLOBAL DRUG DEVELOPMENT

Goals / Definitions

Remove a hazard or reduce the level of its risk by adding precautions or control measure, as necessary.

Design review assessment consists of the identification of hazards and the analysis and evaluation of risks associated with device design.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
• Design risk assessment completed	a) Create a risk management report to capture the combination product's overall residual risk, risk/benefit analysis, and overall conclusion of the product's safety profile. b) Alignment between design output and user needs defined in user requirements specification (URS) c) Refined device design if Instructions for Use cannot mitigate user errors d) Confirmation that intended use statement is defined e) Definition of critical device attributes	

DEVICE DESIGN AND DEVELOPMENT PLAN UPDATED

GLOBAL DRUG DEVELOPMENT

Goals/ Definitions

Update the Design and Development Plan.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
• Design and Development Plan updated	a) Updated Design and Development Plan as data / information becomes available at the appropriate points in the development stage	

DS/DP CHARACTERIZED AT KILO-SCALE

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

To develop the drug substance (DS) and drug product (DP) to provide larger amounts (kilo scale) of clinical trial materials that will be required for Phase 2 studies.

cGMP DS manufactured at kilo-scale and scale-up processes defined.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Drug substance characterization & analytical method development completed/finalized	a) Salt & form selection (e.g., amorphous vs. crystalline, polymorph ID, etc.) b) Structural characterization (e.g., enantiomers, diasteriomers, etc.) c) Chemical purity, impurity characterization, and associated analytical methods d) Stability & shelf life studies (e.g., *T*, pH, humidity, light, etc.) e) Cold chain requirements	▪ Summary of key data to substantiate conclusions ▪ Illustrative data tables or figures may be reported in an appendix
▪ Drug substance manufactured at kilo-scale	a) DS process developed to kilo scale with acceptable yield b) Confirmation of reproducibility of stoichiometry, stable DS physical form and required particle size c) Confirmation of acceptable impurity profile	▪ As above
▪ Drug product characterization & analytical method development completed	a) Delivery & formulation strategy ("light touch" quality-by-design [QbD] approach) to support animal and human studies (e.g., IV, injection, tablet, capsule, pediatric dosage form etc.) b) Particle size considerations and formulation dependency c) Excipient selection and characterization d) Chemical purity, impurity characterization, and associated analytical methods e) Form-specific physicochemical properties (e.g., bulk & tap densities, flowability, compressibility, pXRD, IR, dissolution, disintegration, etc.) f) Form- and formulation-specific stability studies	▪ As above
• GMP Manufacturing	a) Kilo lab GMP DS, Ph 2 DPs Released	▪ Summary of key data, e.g. CoA

Prior to EP1, CMC will ensure that the DS manufacturing process is developed to produce the required salt, form, and purity profile in larger amounts. DP formulation components, manufacturing processes and packaging should be final and scalable so that larger amounts of Phase II clinical study materials can be supplied in a timely manner.

*Candidate progression is discussed at standing grantee update meetings with the investment team

END OF PHASE 1 MEETING SCHEDULED

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Gain concurrence with Regulatory Authority on Phase 2 study design.

End of Phase 1 Meeting (if needed) with FDA/ other NRAs (if applicable) completed.
(*Specific communication requirements of NRAS should be identified upon initiation of the Regulatory Strategy Plan, if pre-IND meeting (or similar NRA meeting) includes a discussion of Phase 2 plans and there is certainty in the path forward/ no protocol adjustments needed based on Phase 1 data / nop regulatory requirement, there may not be a need to conduct a formal End of Phase 1 Meeting with NRAS)

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Data package necessary for End of Phase 1 meeting completed, endorsed, and submitted to NRA	a) Summary of Phase 1 trial results b) Design and scope of Phase 2 study protocol (including study plans, medical monitoring plans, timelines budgets, if required by NRA) c) Proposed clinical development path (e.g. request to use alternate development/authorization pathways (e.g., conditional approval, accelerated, approval, breakthrough designation, orphan designation) and rationale d) Plans for additional nonclinical studies (if any) e) Plans for pediatric studies (including a timeline for protocol finalization, enrollment, completion, and data analysis, or information to support any planned request for waiver or deferral of pediatric studies)	▪ End of Phase 1 briefing package
▪ End of Phase 1 meeting outcomes summarized and development plan modified (if needed)	a) Meeting minutes developed by sponsor and also received from NRA (if possible) with documentation on agreements achieved and agreed next steps/actions in End of Phase 1 meeting b) Revised Phase 2 study protocol c) Revised plans for nonclinical studies, pediatric studies, etc.	▪ Regulatory responses to questions

FORMATIVE HUMAN FACTORS STUDY

GLOBAL DRUG DEVELOPMENT

Goals / Definitions

Conduct Formative Human Factors study and make assessment to modify design as needed.

A study conducted on a combination product prototype user interface at one or more stages during the iterative product development process to assess user interaction with the product and identify potential user errors.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
• Formative Human Factors Study completed	a) Results from Human Factors Studies to optimize the device design b) Updated risk assessments based on the results of these studies and develop risk mitigation strategies as needed c) Modified interface design, Instructions for Use, and/or training to address the problems found d) Re-testing to assess whether mitigation strategies effectively reduced the known risks and did not introduce any new risks	

GLOBAL ACCESS AGREEMENT IN PLACE

GLOBAL DRUG DEVELOPMENT

Goals/ Definitions

Global Access Strategy and Milestones in place

Global Access is commitment from grantees and partners to making the products and information generated by foundation funding widely available at an affordable price, in sufficient volume, at a level of quality, and in a time frame that benefits the people we are trying to help.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Global Access Agreement in place with development partners with commitment to secure commercial and manufacturing partners	• Affirm commitment to a regulatory pathway that enables WHO prequalification • Ensure sufficient drug supply for use in developing countries • Secure affordable pricing for use by intended beneficiaries in developing countries	▪ Global Access commitments should be included in Grant Agreement
▪ Foundation / Grantee agreements in place that provide for Global Access	• Grant Agreement • Global Access Strategy • Data Access Plan • Global Access License • Publication/Open Access • MOU	
▪ Grantee / Third Party agreements in place that provide for Global Access	• Clinical supply agreements • Clinical trial agreements • Technology Transfer agreements • Development Agreements • Regulatory Filings	

IND SUBMITTED TO REGULATORY AGENCY

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Gain concurrence with Regulatory Authority on Phase 1 study design.

Track the regulatory approval to enter to Phase 1 studies.
(*Specific communication requirements of National Regulatory Authorities (NRAs) should be identified in upon initiation of the Regulatory Strategy Plan)

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE

▪ IND application package (or similar NRA clinical trials package) prepared, endorsed, submitted, and received by regulatory agency	• List of regulatory agency requirements (for example)
	  • Drug substance & drug product properties
	  • Stability data
	  • Relevant animal PK and disease model data
	  • Argument for acceptability of preclinical candidate safety profile
	  • Demonstrated in vitro and/or in vivo efficacy/activity, as applicable
	  • Argument for acceptability of drug interaction profile
	  • Feasibility of cGMP manufacture & CMC information relevant to clinical trial supplies
	  • Previous human exposure (if available)
	  • Argument for acceptability of clinical dosage form
	  • Clinical proof of concept plan
	  • Proposed clinical trial protocols
	• Application package aligned with agency requirements
	• Confirmation of application receipt by FDA / NRA
		▪ Notification of submission date

▪ US IND application response (if any) or similar NRA application approved	• If filed with US FDA, confirmation that no response from the US FDA was received within 30 days after the agency's receipt of the IND application • No response confirmation and/or approval confirmation from other NRAs as required for their clinical trials applications • Ethics Committee action	▪ Notification of Regulatory Authority response (if any) and any impact to timeline or study design

PHASE 1 ENDPOINTS MET

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Human safety and dose established.

Phase 1 endpoints met.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Initial safety and tolerability demonstrated (no gross clinical and laboratory abnormalities) relative to the TPP	Satisfactory safety profile using validated methods and adequate statistical analyses: a) Drug-related adverse events (AEs) which may include serious adverse events (SAEs) b) Management of any adverse events (reporting of the events to the applicable ethical committees and regulatory agencies)	▪ Summary of clinical safety data, AEs and SAEs
▪ Phase 1 safety, pharmacokinetics and biomarker data do not preclude the further development of the compound relative to the TPP	a) Validated bioanalytical measurements of drug candidate exposure and relevant biomarker concentrations b) Preliminary exposure-response relationships based on biomarker data	▪ Summary of clinical PK data, exposure, half-life and recommended Phase 2 dose with rationale

PROOF OF CONCEPT OBTAINED

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Data demonstrates that product has expected Mechanism of Action and has potential to meet cTPP.

Drug candidate has demonstrated initial clinical efficacy Proof of Concept.

(*Flexible milestone that may be evaluated at the end of phase 1, phase 2 or phase 3)

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Clinical safety aligns with TPP criteria (includes clinical and laboratory abnormalities)	Satisfactory safety profile using validated assays and adequate statistical analyses a) Safety signal detection (e.g., drug candidate-related adverse events (AEs) which may include serious adverse events (SAEs)) b) Management of any adverse events (reporting of the events to the applicable ethical committees and regulatory agencies)	▪ Summary of data and rationale
▪ Efficacy proof-of-concept completed and aligns with TPP criteria	Initial clinical efficacy proof-of-concept demonstrated using qualified/standardized clinical endpoint assays and adequate statistical analyses	▪ Summary of data and rationale
▪ Exposure-Response characterized to support selection of optimal dosage, regimen, and route of administration for Phase 2 trials defined	a) Exposure-Response characterized b) Dose, regimen, and route of administration studies c) Recommendations for Phase 2 studies	▪ Summary of data and rationale
▪ TPP achievement assessed	a) Probability assessment of whether candidate will meet target product profile	▪ Use cTPP template

REGULATORY STRATEGY AND PLAN

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Regulatory path and plan in place.

Plan for proposed regulatory path through life-cycle of the product.
(*An iterative document that is initiated at FIH, updated continually along the development process and reviewed through to DTF)

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Proposed regulatory path through life-cycle of product defined, including clinical development, licensure, WHO PQ (if needed), and post- authorization safety surveillance and further product development ▪ Include any specific plans to use alternative development pathways (conditional, accelerated, breakthrough) or registration processes (article 58, tropical voucher, orphan)	**a) Prioritized list of countries where the drug is intended to be introduced[1]** **b) Understanding of country-specific regulatory requirements** • Type of submissions (original, supplement/variation, line extension, etc.) • **Significant / unique requirements[2]** • Required HA communications and timing c) Plans for NRA engagement during development to gain feedback and agreement with development and filing strategy d) Key regulatory risks and risk mitigation plans e) Plan to ensure proposed indication and labeling aligns with TPP and donor/utilization requirements **f) Plan for approval and protocol review for clinical trial starts in target countries** **g) Plan to handle monitoring and reporting of adverse events and safety issues during clinical trials and post-authorizations** h) WHO PQ applicability/programmatic suitability, plan to pursue WHO PQ (if applicable) i) Plans for WHO PQ engagement by end of phase 2 (if applicable)	▪ Updated throughout life-cycle of product reflecting new data and priorities as they develop ▪ Required at each gate: Detailed plan with timeline and resources for the next phase of development (e.g. detailed plan for Phase 1 required at the FIH gate review), and high-level / draft plan focusing on risk identification and mitigation for all subsequent phases of development

Items in **bold** font reflect suggested reporting guidelines for this stage gate
[1]If India and China are among the likely target countries, content is required at FIH. Otherwise it applies at EP2.
[2]Specific requirements associated with Chinese Pharmacopeia should be updated early

RUN CLINICAL PROGRAM PHASE 1 (1/2)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Track clinical trial start date.

Track the dosing of the first subject enrolled thereby indicating the beginning of the clinical trial.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Track first dosing event for a patient recruited to the Phase 2 clinical trial	a) Conduct recruitment analysis and compare study starts to the clinical plan b) Inform impact on other planned downstream activities in the case of study start delays	▪ Notification of date first subject dosed and any delay, if incurred

RUN CLINICAL PROGRAM PHASE 1 (2/2)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Track clinical trial start date.

Track the dosing of the first subject enrolled thereby indicating the beginning of the clinical trial.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Track last patient to complete the Phase 2 clinical trial	a) Conduct recruitment analysis and compare study duration to the clinical plan b) Inform impact on other planned downstream activities in the case of study completion delays	▪ Notification of date last subject last visit and any delay, if incurred

STRATEGIC DEMAND FORECAST UPDATED

GLOBAL DRUG DEVELOPMENT

Goals/Definitions

Business case for developing a deliverable product

Business Case, deliverability assessment, strategic demand forecast and COGS reports completed

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE

▪ Strategic Demand Forecast	• An initial, high-level demand forecast will identify:
	  • Target countries
	  • Target sub populations
	  • Timing of introduction specific to identified countries
		▪ BMGF provides methodology

STRATEGIC DEMAND FORECAST UPDATED

GLOBAL DRUG DEVELOPMENT

Goals/Definitions

Business case for developing a deliverable product

Business Case, deliverability assessment, strategic demand forecast and COGS reports completed

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE

▪ Strategic Demand Forecast	• An initial, high-level demand forecast will identify:
	  • Target countries
	  • Target sub populations
	  • Timing of introduction specific to identified countries
		▪ BMGF provides methodology

STUDY START-UP ACTIVITIES INITIATED

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Start-up activities are initiated to enable timely Phase 2 start

Clinical study start-up plan initiated with consideration of feasibility and identification of risks.t

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Clinical trial designed	a) Protocol design and scope for the next phase of development (including study plans, medical monitoring plans, timelines and budgets) to support both NRA approval and WHO PQ b) Proposed clinical development path (i.e., request for conditional approval) and rationales c) Investigator's Brochure updated for the next phase of development. (e.g., prior to First in Human include Core Safety Information from toxicology study) d) At EP2 ensure that feedback/recommendations from engagement with WHO (on target population etc.) are addressed in Phase 3 trial design	▪ Protocol synopsis ▪ Investigator Brochure
▪ Clinical trial site feasibility completed	a) Plan for conducting epidemiology study to understand patient population and identifying potential study sites b) Existing network of investigators and study sites c) Plan for site validation (may include audit) including considerations such as infrastructure, capability, supply chain feasibility, capacity, cGCP certification, etc. d) Understanding of required approval process to conduct clinical studies at all potential study sites and identifying risks e) Data integrity and confidentiality practices	▪ Summary report
▪ Clinical vendors/CRO identified and site initiation activities conducted	a) Scope of work required (e.g., site selection, site initiation, data management, process & method development, etc.) and agreed metrics to monitor trial progress b) Partner engagement strategy (e.g., outsourced activity, insourced activity, consultation, etc.) c) Relationship with local regulatory body, and authorities d) Existing network of investigators and study sites e) Ensure completion of site initiation activities such as: 1) Plan for obtaining Ethical Committee approvals and completing all administrative tasks required to start a clinical study at all study sites; 2) Plan for training of investigators and staff to ensure GCP compliance and protocol compliance (i.e., drug administration, dosing regimen, etc.); 3) Plan for educating patients on protocol compliance (i.e., sample collection, adverse event reporting, etc.); 4) Plan for obtaining Informed Consent with consideration of staff availability and patient literacy	▪ Summary report
▪ Clinical assay readiness	a) Clinical lab identified b) Clinical assays in place prior to entering clinical studies	▪ Summary of assay qualification

UPDATED CANDIDATE TTP

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Candidate Target Product Profile Agreed

The Candidate Target Product Profile (cTTP) describes the desired attributes of the product and are consistent with mechanism of action and preclinical data.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ cTPP further updated to add details	• Drug need, use case, market, and impact on global health • Product characteristics required to show benefit, such as efficacy, safety, and duration of treatment outlined • Primary endpoints and secondary endpoints • Alignment with partner organizations • Manufacturability • Route of administration • Aspirational cost and delivery considerations	▪ Use cTPP template – should reflect the desired Intervention TPP (iTPP)

CLINICAL DEVELOPMENT PLAN UPDATED

GLOBAL DRUG DEVELOPMENT

Goals/ Definitions

Plan for clinical studies for licensure and post-marketing.

Clinical Development Plan initiated

(*Clinical Development Pan is initiated prior to the FIH gate review and is updated & reviewed during development through to the DTF gate review)

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE

▪ Clinical development plan updated	a) Overview of planned clinical activities:
	• Study phase, objectives/research rationale
	• Duration of the studies, number of subjects, recruitment criteria (e.g.,. study arms, patient cohorts, comparators for non-inferiority trials, power calculations etc.)
	• Complete drug-drug interaction and special population place in place
	  • Dosing & dosing modeling strategies
	  • Detailed rationale for Phase 3 dose selection
	  • Toxicology and toxicokinetic results to support doses and dosing duration in Phase 3
	  • Drug combination assessment & plan
	  • Toxicology plan to support submission (e.g., carcinogenicity, reproductive toxicology)
	b) Clinical partners, proposed target countries, and study sites (based on criteria including clinical expertise, sustainability, site capacity, and disease incidence/epidemiology studies, etc.)
	c) Definition of clinical endpoints (primary & secondary), methodology (clinical endpoint assays, data collection plan, statistical methods, etc.), adverse event reporting, stopping rules, etc.
	d) Monitoring, data management, and biostatistics strategies
	e) Post-marketed product surveillance/Phase 4 trial strategy
	f) Mass product administration considerations (e.g., trial design, safety requirements, etc.)
	g) Off-label use considerations
	h) Trial size considerations for diseases with limited incidence rates
	i) Potential risks and mitigation strategies
	j) Timelines and budgets for clinical development
		▪ Detailed Phase 3 clinical plan with timeline
		▪ Updated risk identification and mitigation needed for all subsequent phases of development
		▪ Plans should reflect approaches to accelerate decision making (e.g., adaptive designs, real-time data analysis of clinical trials etc.)
		▪ Phase 3 plan is modified during Phase 2 trial as Phase 2 data become available
		▪ Clinical development plan extends beyond DTF to accommodate the time needed to report Phase 3 results and also cover additional plans for pediatric studies and post-market surveillance

CMC DEVELOPMENT PLAN UPDATED (CP/ADDS) (1 OF 2)

GLOBAL DRUG DEVELOPMENT

Goals/ Definitions

A detailed plan for competing design transfer for the combination product at DTF stage gate.

CMC development plan updated.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ List of activities that will be conducted, that lead to achieving Product Definition and Planning milestone at DTF stage gate	Plans to complete the following bolded items by the next stage gate: • User capabilities and preferences assessment • Ethnographic studies completion • Hazard identification initiation • Concept assessment completion • Design and development plan initiation • Instructions for Use drafts • Human Factors Study Plan • Application risk assessment completion • Design History File initiation • Design Input Review completion • High-level Project Plan and definition of critical product attributes (if prototype available) • Preliminary device prototype generation • Design Output Review completion • Formative human factors study completion • Design risk assessment completion • Process risk assessment initiated • Critical component dimensions and specifications definition • Design and Development Plan updates • Instructions for Use updates • Design History File updates • Engineering testing of prototype and conduct simulated use or clinical testing • Summative human factors study initiated • Design verification execution • Design Verification Review completion • Design validation execution • Design Validation Review completion • Design transfer completion • Design Transfer Review completion • Supply chain / logistics plan completion • Complaint handling process definition • Pharmacovigilance plan completion	▪ A detailed plan to achieve the FIH CMC milestones is expected ▪ Additionally, the plan should identify potential development risks to launch and risk mitigation strategies related to development timeline, costs, and resource allocation

CMC DEVELOPMENT PLAN UPDATED (CP/ADDS) (2 OF 2)

GLOBAL DRUG DEVELOPMENT

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
• Instructions for Use updated	a) Updated Instructions for Use as data/information becomes available at the appropriate points in the development stage	▪ Summary report containing key data / information to substantiate conclusions ▪ Illustrative data tables or figures may be reported in an appendix
• Process risk assessment completed	a) Critical molding and assembly process parameters b) Identification of CMOs and assessment of impact on manufacturing costs and COGS c) Creation of manufacturing flow diagram and assess product demand to verify COGS based on projected demand forecast	
• Review TPP	a) Review TPP developed and determine if modifications are necessary	

CMC DEVELOPMEN PLAN UPDATED (CP-ADDS) (1 OF 2)

GLOBAL DRUG DEVELOPMENT

Goals/ Definitions

A detailed plan for competing design transfer for the combination product at DTF stage gate.

CMC development plan updated.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ List of activities that will be conducted, that lead to achieving Product Definition and Planning milestone at DTF stage gate	Plans to complete the following bolded items by the next stage gate: • User capabilities and preferences assessment • Ethnographic studies completion • Hazard identification initiation • Concept assessment completion • Design and development plan initiation • Instructions for Use drafts • Human Factors Study Plan • Application risk assessment completion • Design History File initiation • Design Input Review completion • High-level Project Plan and definition of critical product attributes(if prototype available) • Preliminary device prototype generation • Design Output Review completion • Formative human factors study completion • Design risk assessment completion • Process risk assessment initiated • Critical component dimensions and specifications definition • Design and Development Plan updates • Instructions for Use updates • Design History File updates • Engineering testing of prototype and conduct simulated use or clinical testing • Summative human factors study initiated • Design verification execution • Design Verification Review completion • Design validation execution • Design Validation Review completion • **Design transfer completion** • **Design Transfer Review completion** • **Supply chain / logistics plan completion** • Complaint handling process definition • Pharmacovigilance plan completion	▪ A detailed plan to achieve the FIH CMC milestones is expected ▪ Additionally, the plan should identify potential development risks to launch and risk mitigation strategies related to development timeline, costs, and resource allocation

* Items in **bold** font reflect suggested reporting guidelines for this stage gate

CMC DEVELOPMEN PLAN UPDATED (CP-ADDS) (2 OF 2)

GLOBAL DRUG DEVELOPMENT

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Instructions for Use updated	a) Updated Instructions for Use as data/information becomes available at the appropriate points in the development stage	▪ Summary report containing key data / information to substantiate conclusions ▪ Illustrative data tables or figures may be reported in an appendix
▪ Process risk assessment completed	a) Critical molding and assembly process parameters b) Identification of CMOs and assessment of impact on manufacturing costs and COGS c) Creation of manufacturing flow diagram and assess product demand to verify COGS based on projected demand forecast	
▪ Review TPP	a) Review TPP developed and determine if modifications are necessary	

*Candidate progression is discussed at standing grantee update meetings with the investment team

CMC DEVELOPMENT PLAN UPDATED (DRUGS)

GLOBAL DRUG DEVELOPMENT

Goals/ Definitions

A detailed plan to address post-launch support – including technical issues during manufacturing and ongoing interactions with regulatory authorities.

CMC development plan updated.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ List of activities that will be conducted, that lead to achieving the "Full-Scale Post-Launch Manufacturing Strategy In Place" milestone at DTF stage gate	• Complete initial drug product characterization • Define cGMP manufacturing process • Complete GMP manufacturing for Ph 1 • Finalize DS characterization & analytical method development • Manufacture DS at kilo-scale • Complete DP characterization • Complete DP package characterization • Manufacture DP to support the Phase 2 clinical trial • Manufacturing process optimization • GMP manufacturing for Ph 3 • Readiness for Tech Transfer • Technology transfer and validation of raw material, drug substance, and drug product analytical and functional release testing • Technology transfer and validation of drug substance & drug product manufacturing and packaging processes • Qualification of commercial-scale facilities • **Commercial launch strategy** • **QA/compliance activities** • **Ongoing CMC Support to ensure uninterrupted supply of high quality DP in all markets**	▪ A detailed plan to achieve the DTF CMC milestones is expected ▪ Additionally, the Plan should identify potential development risks to PQ, and risk mitigation strategies related to development timeline, costs and resource allocation

* Items in **bold** font reflect suggested reporting guidelines for this stage gate

COGS UPDATED

GLOBAL DRUG DEVELOPMENT

Goals/Definitions

Business case for developing a deliverable product

Identification of commercial partner(s) for launch and full-scale manufacturing of the product

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ COGS	A COGS analysis at EP2 will identify: a) Product price, volume, and revenue based on commercial scale production b) Variable and fixed costs for R&D, facilities, equipment, labor, and raw materials c) Licensing expenses and incomes d) Grants, loans and outstanding debts related to the product e) Related product sales f) Projected price (within 30% of TPP target)	▪ BMGF provides methodology

COMMERCIAL PARTNER IDENTIFIED

GLOBAL DRUG DEVELOPMENT

Goals / Definition

Rationale and justification for selection of commercial partner.

Identification of commercial partner(s) for launch and full-scale manufacturing of the product.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Partner (commercial, government, non-profit, etc.) assessments to determine the fit for collaboration completed	a) Respective expectations and business model (i.e., pricing of drug pricing upon licensure, IP control, etc.) b) Mid- to long-term strategic fit (i.e., intent for pursuit of the product over mid/long term to ensure the viability of the product development and partnership) c) Assess whether the NRA in the manufacturer's country is considered a functional NRA by the WHO d) Identify timing of decision points where contingency plan needs to be triggered if suitable commercial partner is not selected	▪ Summary of key data and rationale to support partner selection ▪ Additional detail may be reported in an appendix

COST-EFFECTIVENESS ANALYSIS UPDATED

GLOBAL DRUG DEVELOPMENT

Goals/Definitions

Business case for developing a deliverable product

Identification of commercial partner(s) for launch and full-scale manufacturing of the product

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Cost-Effectiveness Analysis	A cost-effectiveness analysis at EP2 will identify: a) Limitations of economic evaluations performed b) Comparators and mean costs and effects of the product and the competitor c) Cost and effects of the product on sub-populations d) Groups that may be disproportionally impacted positively or negatively	▪ BMGF provides methodology

DELIVERABILITY ASSESSMENT UPDATED

GLOBAL DRUG DEVELOPMENT

Goals/Definitions

Business case for developing a deliverable product

Identification of commercial partner(s) for launch and full-scale manufacturing of the product

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Deliverability Assessment	The delivery plan will summarize: a) Regulatory plan and first-wave country partners b) Production/manufacturing partners with projected product price, volume, and revenue c) Country supply chain and user targeting methodology d) Roll-out plans for first-wave countries e) Country decision support plans that verify capacity, resources, and new technologies for introduction f) Global policy and initiative opportunities/partnerships g) Benefits over current standard of care h) Global policy milestones and pathway identified to reach critical registration (i.e., PQ, EMA)	▪ Summary report

DELIVERY MILESTONES FOR DECISION TO ENTER PHASE 3 TRIALS (1/2)

GLOBAL DRUG DEVELOPMENT

Goals / Definition

Business case for developing a deliverable product.

Identification of commercial partner(s) for launch and full-scale manufacturing of the product.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Deliverability Assessment	The delivery plan will summarize: a) Regulatory plan and first-wave country partners b) Production/manufacturing partners with projected product price, volume, and revenue c) Country supply chain and user targeting methodology d) Roll-out plans for first-wave countries e) Country decision support plans that verify capacity, resources, and new technologies for introduction f) Global policy and initiative opportunities/partnerships g) Benefits over current standard of care h) Global policy milestones and pathway identified to reach critical registration (i.e., PQ, EMA)	▪ Summary report
▪ Strategic Demand Forecast	The demand forecast at EP2 will include: a) Target countries for introduction b) Target populations/sub-populations c) Timing and speed of introduction specific to identified countries d) Product accessibility and availability e) Predicted coverage rate f) Expected volumes and pricing g) Sensitivity analysis based on key assumptions and drivers of forecast	▪ BMGF provides methodology

Goals / Definition

Business case for developing a deliverable product.
Identification of commercial partner(s) for launch and full-scale manufacturing of the product.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ COGS	A COGS analysis at EP2 will identify: a) Product price, volume, and revenue based on commercial scale production b) Variable and fixed costs for R&D, facilities, equipment, labor, and raw materials c) Licensing expenses and incomes d) Grants, loans and outstanding debts related to the product e) Related product sales f) Projected price (within 30% of TPP target)	▪ BMGF provides methodology
▪ Cost-Effectiveness Analysis	A cost-effectiveness analysis at EP2 will identify: a) Limitations of economic evaluations performed b) Comparators and mean costs and effects of the product and the competitor c) Cost and effects of the product on sub-populations d) Groups that may be disproportionally impacted positively or negatively	▪ BMGF provides methodology
▪ Launch Budget Prediction	The first iteration of the launch budget prediction will include: a) An estimate of the scale of launch support and budget for successful uptake b) Detailed budget for pre-launch activities	▪ Draft launch budget

DELIVERY MILESTONES FOR DECISION TO ENTER PHASE 3 TRIALS (1/2)

GLOBAL DRUG DEVELOPMENT

Goals / Definition

Business case for developing a deliverable product.
Identification of commercial partner(s) for launch and full-scale manufacturing of the product.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Deliverability Assessment	The delivery plan will summarize: a) Regulatory plan and first-wave country partners b) Production/manufacturing partners with projected product price, volume, and revenue c) Country supply chain and user targeting methodology d) Roll-out plans for first-wave countries e) Country decision support plans that verify capacity, resources, and new technologies for introduction f) Global policy and initiative opportunities/partnerships g) Benefits over current standard of care h) Global policy milestones and pathway identified to reach critical registration (i.e., PQ, EMA)	▪ Summary report
▪ Strategic Demand Forecast	The demand forecast at EP2 will include: a) Target countries for introduction b) Target populations/sub-populations c) Timing and speed of introduction specific to identified countries d) Product accessibility and availability e) Predicted coverage rate f) Expected volumes and pricing g) Sensitivity analysis based on key assumptions and drivers of forecast	▪ BMGF provides methodology

Goals / Definition

Business case for developing a deliverable product.
Identification of commercial partner(s) for launch and full-scale manufacturing of the product.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ COGS	A COGS analysis at EP2 will identify: a) Product price, volume, and revenue based on commercial scale production b) Variable and fixed costs for R&D, facilities, equipment, labor, and raw materials c) Licensing expenses and incomes d) Grants, loans and outstanding debts related to the product e) Related product sales f) Projected price (within 30% of TPP target)	▪ BMGF provides methodology
▪ Cost-Effectiveness Analysis	A cost-effectiveness analysis at EP2 will identify: a) Limitations of economic evaluations performed b) Comparators and mean costs and effects of the product and the competitor c) Cost and effects of the product on sub-populations d) Groups that may be disproportionally impacted positively or negatively	▪ BMGF provides methodology
▪ Launch Budget Prediction	The first iteration of the launch budget prediction will include: a) An estimate of the scale of launch support and budget for successful uptake b) Detailed budget for pre-launch activities	▪ Draft launch budget

DESIGN HISTORY FILE UPDATED

GLOBAL DRUG DEVELOPMENT

Goals / Definition

To update the compilation of documentation that describes the design history of a finished medical device.

The DHF contains or references the records necessary to demonstrate that the design was developed in accordance with the approved design plan.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
• Design History File updated	a) Updated Design History File as data/information becomes available at the appropriate points in the development stage b) Changes made to product need to be captured within the Design History File	

DESIGN VERIFICATION AND VALIDATION REVIEWS

GLOBAL DRUG DEVELOPMENT

Goals / Definition

To confirm that the design output meets the design input requirements.

Objective evidence, in the form of validation testing, to ensure that product design meets specifications, government/ industry requirement, and user needs.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Design verification executed	a) Execute design verification based on in-process controls and monitoring plan b) Validate analytical tests and methods c) Conduct transportation and stability testing studies d) Initiate documentation of Design Validation Master File, including protocols for Factory Acceptance Tests / Site Acceptance Tests and Installation Qualification / Operational Qualification	e) Summary report containing key data / information to substantiate conclusions f) Illustrative data tables or figures may be reported in an appendix
▪ Design Verification Review conducted	g) Conclusions and recommendations from the Design Verification Review h) Control plans updated based on risk assessment and Design Verification Review	
▪ Design validation executed	i) Execute design validation based on in-process controls and monitoring plan j) Validate analytical tests and methods k) Conduct transportation and stability testing studies l) Validate molding and assembly process by demonstration of full functionality against design input requirement	
▪ Design Validation Review conducted	m) Conclusions and recommendations from the Design Validation Review n) Control plans updated based on risk assessment and Design Validation Review	

*Candidate progression is discussed at standing grantee update meetings with the investment team

Goals / Definition

Update the Design and Development Plan

Establish and maintain plans that: (1) Describe or reference design and development activities. (2) Define responsibility for implementation. (3) Identify or describe interfaces with different groups or activities. (4) Review, document, update and approve plans as design and development evolves.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Design and Development Plan updated	a) Updated Design and Development Plan as data / information becomes available at the appropriate points in the development stage	

END OF PHASE 2 MEETING PLANNED OR SCHEDULED*

GLOBAL DRUG DEVELOPMENT

Goals/ Definitions

Gain concurrence with Regulatory Authority on Phase 3 study design.
End of Phase 2 Meeting with NRAs (if applicable) completed.
(*Specific communication requirements of NRAs should be identified upon initiation of the Regulatory Strategy Plan)

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Data package necessary for End of Phase 2 meeting completed and submitted to NRA	a) Summaries of Phase 1/2 trial results b) Design and scope of Phase 3 study protocol (including study plans, medical monitoring plans, timelines and, if required by NRA, budgets) c) Plans for any additional nonclinical studies d) Review/update plans for pediatric studies (including a time line for protocol finalization, enrollment, completion, and data analysis, or information to support any planned request for waiver or deferral of pediatric studies) e) Identification of relevant product issues (i.e., plans to manufacturing scale-up to produce product for commercial scale and the need for comparability testing relative to the product used in Phase 1/2 clinical studies) f) Planned label, especially highlighting desired wording for indications (s) and any safety claims desired to make If a Special Protocol Assessment agreement is desired (US specific), also requires: a) Detailed protocol design (i.e., proposed size, power calculation, choice of study endpoints, choice of control, duration, methods of assessment) b) Data analysis plan c) Role of the study in the overall development plan	▪ End of Phase 2 briefing package
▪ End of Phase 2 meeting outcomes summarized and development plan modified (if needed)	a) Meeting minutes prepared by sponsor and shared with NRA; get NRA minutes (if possible). Document agreements achieved and next steps/actions agreed at end of Phase 2 meeting b) Revised Phase 3 study protocol c) Revised plans for nonclinical studies or pediatric studies	▪ Regulatory responses to questions

FULL-SCALE DS/DP MANUFACTURING PROCESS OPTIMIZED

GLOBAL DRUG DEVELOPMENT

Goals/ Definitions

The development and optimization of the manufacturing process to ensure that the drug substance and product used in the pivotal Phase 3 trial are representative of future commercial product quality.

Manufacturing process developed and scaled up.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Manufacturing process optimization completed	a) Design-of-experiments and quality-by-design (QbD) methodology with consideration given with ICH Q8, Q9 and Q10 guidance b) Drug substance manufacturing process optimization, scale-up, and pilot studies (e.g., modification of synthetic pathways, intermediate selection, selection of unit operations and equipment, purification process refinement, etc.) c) Drug product manufacturing process optimization, scale-up, and pilot studies (e.g., selection of unit operations to support desired formulation, blending process refinement, etc.) d) Packaging line equipment selection, trials, and optimization e) Process flow diagrams and draft operating parameters f) Operating parameter (yield, purity, and form) relationships g) Waste reduction strategy and product/package end-of-life considerations h) Re-packaging considerations (e.g., end-use packaging vs. packaging for re-distribution)	▪ Summary of key data to substantiate conclusions ▪ Illustrative data tables or figures may be reported in an appendix
▪ Commercial-scale drug manufacturing feasibility assessment completed	a) Evaluation of pilot plant results (product and process) including process economics (e.g. COGs) to make any corrections and a decision on whether or not to proceed with a full-scale plant development b) Safety and ecological assessment of processing and effluents	▪ As above
▪ Drug product package characterization completed	a) Leachable/extractable assessment b) Child resistant/senior friendliness testing c) Tamper evidence d) Product compatibility (from package and from environment)	▪ As above
▪ GMP Manufacturing	a) GMP Ph 3 DS and DPs released	▪ Summary of key data, e.g. CoA

*Candidate progression is discussed at standing grantee update meetings with the investment team

** If a commercial partner has not been identified by EP2, either the PDP will commercialize the products or, PDP will secure adequate funding to conduct future CMC activities

GLOBAL ACCESS AGREEMENT IN PLACE

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Global Access Commitment Agreement in place.

Global Access is commitment from grantees and partners to making the products and information generated by foundation funding widely available at an affordable price, in sufficient volume, at a level of quality, and in a time frame that benefits the people we are trying to help.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Global Access agreement in place with development partners and negotiation should be on track for potential commercial and manufacturing partners	• Affirm commitment to a regulatory pathway that enables WHO prequalification • Ensure sufficient drug supply for use in developing countries • Secure affordable pricing for use by intended beneficiaries in developing countries	▪ Global Access commitments should be included in Grant Agreement
▪ Foundation / Grantee agreements in place that provide for Global Access	• Grant Agreement • Global Access Agreement • Price & Volume commitments • Volume Guarantee/Loan/PRI • Global Access License • Requirement to seek WHO PQ	
▪ Grantee / Third Party agreements in place that provide for Global Access	• Clinical supply agreements • Clinical trial agreements • Technology Transfer agreements • Development Agreements • Regulatory Filings	

LAUNCH BUDGET PREDICTION

GLOBAL DRUG DEVELOPMENT

Goals/Definitions

Business case for developing a deliverable product

Identification of commercial partner(s) for launch and full-scale manufacturing of the product

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Launch Budget Prediction	The first iteration of the launch budget prediction will include: a) An estimate of the scale of launch support and budget for successful uptake b) Detailed budget for pre-launch activities	▪ Draft launch budget

PROOF OF CONCEPT OBTAINED

GLOBAL DRUG DEVELOPMENT

Goals/ Definitions

Data demonstrating Proof of Conceptand that product and has potential to meetcTPP

Drug candidate has demonstrated initial clinical efficacy Proof of Concept.
(*Flexible milestone that may be evaluated at the end of phase 1, phase 2a, or phase 2b)

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Clinical safety aligns with TPP criteria (includes clinical and laboratory abnormalities)	Satisfactory safety profile using validated assays and adequatestatistical analyses a) Safety signal detection (e.g., drug candidate-related adverseevents (AEs) which may includeserious adverse events (SAEs)) b) Management of any adverse events (reporting of the events to the applicableethical committees and regulatory agencies)	▪ Summary of data and rationale
▪ Efficacy proof-of-concept completed and aligns with TPP criteria	Initial clinical efficacy proof-of-concept demonstrated using qualified/standardized clinical endpoint assays and adequate statistical analyses a) Efficacy (either clinical diseaseor infection) in Phase 2a and/or Phase 2b studies in endemic populations b) Superiority or non-inferiority data in comparativestudies against licensed drug (or treatment) control (if applicable)	▪ Summary of data and rationale
▪ Exposure-Response characterized to support selection of optimal dosage, regimen, and route of administration for Phase 3 trials defined	a) Exposure-Response characterized b) Dose, regimen, and route of administration studies c) Recommendations for Phase 3 studies	▪ Summary of data and rationale
▪ TPP achievement assessed	a) Probability assessment of whether candidatewill meet target product profile	▪ Use cTPPtemplate

REGULATORY STRATEGY AND PLAN UPDATED

GLOBAL DRUG DEVELOPMENT

Goals/ Definitions

Regulatory path and plan in place.
Plan for proposed regulatory path through life-cycle of the product
(*An iterative document that is initiated at FIH, updated continually along the development process, and reviewed through to DTF)

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Proposed regulatory path through life-cycle of product defined, including clinical development, licensure, WHO PQ (if needed), and post-authorization safety surveillance and further product development ▪ Include any specific plans to use alternative development pathways (conditional, accelerated, breakthrough) or registration processes (article 58, tropical voucher, orphan)	**a) Prioritized list of countries where the drug is intended to be introduced** **b) Understanding of country-specific regulatory requirements** • **Type of submissions (original, supplement/variation, line extension, etc)** • **Significant / unique requirements** • **Required HA communications and timing** **c) Plans for NRA engagement during development to gain feedback and agreement with development and filing strategy** **d) Key regulatory risks and risk mitigation plans** **e) Plan to ensure proposed indication and labeling aligns with TPP and donor/utilization requirements** **f) Plan for approval and protocol review for clinical trial starts in target countries** **g) Plan to handle monitoring and reporting of adverse events and safety issues during clinical trials and post-authorizations** **h) WHO PQ applicability/programmatic suitability, plan to pursue WHO PQ (if applicable)** i) **Plans for WHO PQ engagement by end of phase 2 (if applicable)**	▪ Updated throughout life-cycle of product reflecting new data and priorities as they develop ▪ Required at each gate: Detailed plan with timeline and resources for the next phase of development (e.g. detailed plan for Phase 1 required at the FIH gate review), and high-level / draft plan focusing on risk identification and mitigation for all subsequent phases of development

*Items in **bold** font reflect suggested reporting guidelines for this stage gate

RUN CLINICAL PROGRAM PHASE 1 (1/4)

GLOBAL DRUG DEVELOPMENT

Goals/ Definitions

Track clinical trial start date.

Track the dosing of the first subject enrolled thereby indicating the beginning of the clinical trial.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Track first dosing event for a patient recruited to the Phase 3 clinical trial	a) Conduct recruitment analysis and compare study starts to the clinical plan b) Inform impact on other planned downstream activities in the case of study start delays	▪ Notification of date first subject dosed and any delay, if incurred

RUN CLINICAL PROGRM PHASE 2 (1/4)

GLOBAL DRUG DEVELOPMENT

Goals/ Definitions

Track clinical trial start date.

Track the dosing of the first subject enrolled thereby indicating the beginning of the clinical trial.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Track first dosing event for a patient recruited to the Phase 3 clinical trial	a) Conduct recruitment analysis and compare study starts to the clinical plan b) Inform impact on other planned downstream activities in the case of study start delays	▪ Notification of date first subject dosed and any delay, if incurred

RUN CLINICAL PROGRM PHASE 2 (2/4)

GLOBAL DRUG DEVELOPMENT

Goals/ Definitions

Track that enrolment in the clinical trial is proceeding according to plan.

Track the progress and feasibility of Phase 3 clinical trials.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
• Track recruitment and budget by comparing actual patient enrollment to previously established benchmarks at 25% of the projected recruitment period	a) Conduct recruitment analysis and report number of patients recruited and budget within 25% of the projected recruitment period b) If suboptimal recruitment is identified, submit an analysis of recruitment barriers and a corrective recruitment plan with revised budget and timeline c) If recruitment levels are below minimum acceptable levels: evaluate feasibility to complete study within acceptable budget or timeframe and submit corrective recruitment plan	▪ Notification of milestone achievement, any delay, mitigations and revised timeline

RUN CLINICAL PROGRM PHASE 2 (3/4)

GLOBAL DRUG DEVELOPMENT

Goals/ Definitions

Check that data quality is on track to meet target clinical study report date.

Monitor data cleaning process to expedite database lock, data analysis, and data submission.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Initiate datacleaning process as data becomes availableto allow accessto high integrity and quality data and expedite data analysis and submission *NOTE: Data cleaning process and plan should be clearly defined at the beginning of the study. Readiness for database lock should be considered at patient level and entire data base level.*	a) Streamlined datacleaning process to expedite clinical dataanalysis and submission b) Provide estimated time to database lock, dataanalysis, and datasubmission c) Report SAEs and any otherissues	▪ Notification of milestone achievement, anydelay, mitigations and revised timeline

RUN CLINICAL PROGRM PHASE 2 (3/4)

GLOBAL DRUG DEVELOPMENT

Goals/ Definitions

Track Clinical Trial end date.

Track the date for the last subject to complete the trial thereby indicating the end of the clinical trial.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Track last patient to complete the Phase 3 clinical trial	a) Conduct recruitment analysis and compare study duration to the clinical plan b) Inform impact on other planned downstream activities in the case of study completion delays	▪ Notification of date last subject last visit and any delay, if incurred

RUN CLINICAL PROGRAM PHASE 2 (2/4)

GLOBAL DRUG DEVELOPMENT

Goals/ Definitions

Track that enrolment in the clinical trial is proceeding according to plan.

Track the progress and feasibility of Phase 3 clinical trials.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
• Track recruitment and budget by comparing actual patient enrollment to previously established benchmarks at 25% of the projected recruitment period	a) Conduct recruitment analysis and report number of patients recruited and budget within 25% of the projected recruitment period b) If suboptimal recruitment is identified, submit an analysis of recruitment barriers and a corrective recruitment plan with revised budget and timeline c) If recruitment levels are below minimum acceptable levels: evaluate feasibility to complete study within acceptable budget or timeframe and submit corrective recruitment plan	▪ Notification of milestone achievement, any delay, mitigations and revised timeline

RUN CLINICAL PROGRAM PHASE 2 (3/4)

GLOBAL DRUG DEVELOPMENT

Goals/ Definitions

Check that data quality is on track to meet target clinical study report date.

Monitor data cleaning process to expedite database lock, data analysis, and data submission.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Initiate data cleaning process as data becomes available to allow access to high integrity and quality data and expedite data analysis and submission *NOTE: Data cleaning process and plan should be clearly defined at the beginning of the study. Readiness for database lock should be considered at patient level and entire data base level.*	a) Streamlined data cleaning process to expedite clinical data analysis and submission b) Provide estimated time to database lock, data analysis, and data submission c) Report SAEs and any other issues	▪ Notification of milestone achievement, any delay, mitigations and revised timeline

RUN CLINICAL PROGRAM PHASE 2 (4/4)

GLOBAL DRUG DEVELOPMENT

Goals/ Definitions

Track Clinical Trial end date.

Track the date for the last subject to complete the trial thereby indicating the end of the clinical trial.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Track last patient to complete the Phase 3 clinical trial	a) Conduct recruitment analysis and compare study duration to the clinical plan b) Inform impact on other planned downstream activities in the case of study completion delays	▪ Notification of date last subject last visit and any delay, if incurred

RUN CLINICAL PROGRAM PHASE 2 (1/4)

GLOBAL DRUG DEVELOPMENT

Goals/ Definitions

Track clinical trial start date.

Track the dosing of the first subject enrolled thereby indicating the beginning of the clinical trial.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Track first dosing event for a patient recruited to the Phase 3 clinical trial	a) Conduct recruitment analysis and compare study starts to the clinical plan b) Inform impact on other planned downstream activities in the case of study start delays	▪ Notification of date first subject dosed and any delay, if incurred

RUN CLINICAL PROGRAM PHASE 2 (2/4)

GLOBAL DRUG DEVELOPMENT

Goals/ Definitions

Track that enrolment in the clinical trial is proceeding according to plan.

Track the progress and feasibility of Phase 3 clinical trials.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
• Track recruitment and budget by comparing actual patient enrollment to previously established benchmarks at 25% of the projected recruitment period	a) Conduct recruitment analysis and report number of patients recruited and budget within 25% of the projected recruitment period b) If suboptimal recruitment is identified, submit an analysis of recruitment barriers and a corrective recruitment plan with revised budget and timeline c) If recruitment levels are below minimum acceptable levels: evaluate feasibility to complete study within acceptable budget or timeframe and submit corrective recruitment plan	▪ Notification of milestone achievement, any delay, mitigations and revised timeline

RUN CLINICAL PROGRAM PHASE 2 (3/4)

Goals/ Definitions

Check that data quality is on track to meet target clinical study report date.

Monitor data cleaning process to expedite database lock, data analysis, and data submission.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Initiate data cleaning process as data becomes available to allow access to high integrity and quality data and expedite data analysis and submission *NOTE: Data cleaning process and plan should be clearly defined at the beginning of the study. Readiness for database lock should be considered at patient level and entire data base level.*	a) Streamlined data cleaning process to expedite clinical data analysis and submission b) Provide estimated time to database lock, data analysis, and data submission c) Report SAEs and any other issues	▪ Notification of milestone achievement, any delay, mitigations and revised timeline

RUN CLINICAL PROGRAM PHASE 2 (4/4)

Goals/ Definitions

Track Clinical Trial end date.

Track the date for the last subject to complete the trial thereby indicating the end of the clinical trial.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Track last patient to complete the Phase 3 clinical trial	a) Conduct recruitment analysis and compare study duration to the clinical plan b) Inform impact on other planned downstream activities in the case of study completion delays	▪ Notification of date last subject last visit and any delay, if incurred

STRATEGIC DEMAND FORECAST UPDATED

GLOBAL DRUG DEVELOPMENT

Goals/Definitions

Business case for developing a deliverable product

Identification of commercial partner(s) for launch and full-scale manufacturing of the product

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Strategic Demand Forecast	The demand forecast at EP2 will include: a) Target countries for introduction b) Target populations/sub-populations c) Timing and speed of introduction specific to identified countries d) Product accessibility and availability e) Predicted coverage rate f) Expected volumes and pricing g) Sensitivity analysis based on key assumptions and drivers of forecast	▪ BMGF provides methodology

STRATEGIC DEMAND FORECAST

GLOBAL DRUG DEVELOPMENT

Goals/Definitions

Business case for developing a deliverable product

Identification of commercial partner(s) for launch and full-scale manufacturing of the product

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Strategic Demand Forecast	The demand forecast at EP2 will include: a) Target countries for introduction b) Target populations/sub-populations c) Timing and speed of introduction specific to identified countries d) Product accessibility and availability e) Predicted coverage rate f) Expected volumes and pricing g) Sensitivity analysis based on key assumptions and drivers of forecast	▪ BMGF provides methodology

STUDY START-UP ACTIVITIES INITIATED

GLOBAL DRUG DEVELOPMENT

Goals/ Definitions

Start-up activities are initiated to enable timely Phase 3 start.
Clinical study start-up plan initiated with consideration of feasibility and identification risks.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Clinical trial designed	a) Protocol design and scope for the next phase of development (including study plans, medical monitoring plans, timelines and budgets) to support both NRA approval and WHO PQ b) Proposed clinical development path (i.e., request for conditional approval) and rationales c) Investigator's Brochure updated for the next phase of development. (e.g., prior to First in Human include Core Safety Information from toxicology study) d) At EP2 ensure that feedback/recommendations from engagement with WHO (on target population etc.) are addressed in Phase 3 trial design	▪ Phase 3 protocol and IB
▪ Clinical trial site feasibility completed	a) Plan for conducting epidemiology study to understand patient population and identifying potential study sites b) Existing network of investigators and study sites c) Plan for site validation (may include audit) including considerations such as infrastructure, capability, supply chain feasibility, capacity, cGCP certification, etc. d) Understanding of required approval process to conduct clinical studies at all potential study sites and identifying risks e) Data integrity and confidentiality practices	▪ List of sites, risks and mitigations
▪ Clinical vendors/CRO identified and site initiation activities conducted	a) Scope of work required (e.g., site selection, site initiation, data management, process & method development, etc.) and agreed metrics to monitor trial progress b) Partner engagement strategy (e.g., outsourced activity, insourced activity, consultation, etc.) c) Relationship with local regulatory body, and authorities d) Existing network of investigators and study sites e) Ensure completion of site initiation activities such as: 1) Plan for obtaining Ethical Committee approvals and completing all administrative tasks required to start a clinical study at all study sites; 2) Plan for training of investigators and staff to ensure GCP compliance and protocol compliance (i.e., drug administration, dosing regimen, etc.); 3) Plan for educating patients on protocol compliance (i.e., sample collection, adverse event reporting, etc.); 4) Plan for obtaining Informed Consent with consideration of staff availability and patient literacy	▪ Summary and start-up timelines
▪ Clinical assay readiness	a) Clinical lab identified b) Clinical assays in place prior to entering clinical studies	▪ Summary of assay validation

SUMMATIVE HUMAN FACTORS STUDY COMPLETED

GLOBAL DRUG DEVELOPMENT

Goals / Definition

Conduct Summative Human Factors Study and compile final results.

This test validates that the device, product or system is safe, effective and usable by the all intended user groups. It differs from the formative test in that now you have to use a device that represents exactly the device that is going to be launched to the market.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Summative Human Factors study completed	a) Provide evidence of safety and efficacy of the drug-device combination product – from use by representative intended users, under realistic use conditions, for essential and high-risk tasks b) Observe and record errors and/or failures using objective and subjective measures c) Collect user opinion and feedback, particularly related to use problems	

UPDATED CANDIDATE TPP

GLOBAL DRUG DEVELOPMENT

Goals/ Definitions

Candidate Target Product Profile Agreed.

Identification of commercial partner(s) for launch and full-scale manufacturing of the product.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Updated cTPP with further details	a) Indication, use case, and target population b) Global health impact c) Proposed mechanism of action d) Primary endpoints and secondary endpoints e) Manufacturability f) Formulation, dosing, and stability g) Route of administration h) Shelf-life and storage i) Cost and delivery considerations j) Product registration strategy	▪ Use cTPP template – should reflect the desired Intervention TPP (iTPP)

CLINICAL DEVELOPMENT PLAN UPDATED

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Clinical safety data and rationale for registration.

Clinical Development Plan initiated.

(*Clinical Development Plan is initiated prior to the FIH gave review and is updated & reviewed during development through to the DTF gate review)

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Clinical development plan initiated	a) Overview of planned clinical activities post-approval: • Study phase, objectives/research rationale • Duration of the studies, number of subjects, recruitment criteria (e.g.,. study arms, patient cohorts, comparators for non-inferiority trials, power calculations etc.) • **Special populations dosing & dosing modeling strategies** • **New formulation assessment & plan** b) Clinical partners, proposed target countries, and study sites (based on criteria including clinical expertise, sustainability, site capacity, and disease incidence/epidemiology studies, etc.) c) Post-marketed product surveillance/Phase 4 trial strategy d) Mass product administration considerations (e.g., trial design, safety requirements, etc.) e) Off-label use considerations f) Trial size considerations for diseases with limited incidence rates g) Potential risks and mitigation strategies h) Timelines and budgets for post-approval clinical development	▪ Detailed post approval clinical plan with timeline ▪ Risk identification and mitigation needed for post approval phase of development ▪ **Post approval Clinical Development Plan should be finalized prior to the DTF gate review (i.e., prior to registration)** ▪ Clinical Development Plan extends beyond DTF gate to accommodate time needed to report Phase 3 results and also to cover additional plans for pediatric studies and post-market surveillance

* Items in **bold** font reflect suggested reporting guidelines for this stage gate

CMC DEVELOPMENT PLAN UPDATED (CP/ADDS)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

A detailed plan for completing Post-Launch Surveillance Plan for the combination product at PQ/LR gate.
CMC development plan updated.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE

▪ List of activities that will be conducted, that lead to achieving Product Definition and Planning milestone at PQ/LR stage gate	Plans to complete the following bolded items by the next stage gate:
	• User capabilities and preferences assessment
	• Ethnographic studies completion
	• Hazard identification initiation
	• Concept assessment completion
	• Design and development plan initiation
	• Instructions for Use drafts
	• Human Factors Study Plan
	• Application risk assessment completion
	• Design History File initiation
	• Design Input Review completion
	• High-level Project Plan and definition of critical product attributes (if prototype available)
	• Preliminary device prototype generation
	  • Design Output Review completion
	  • Formative human factors study completion
	  • Design risk assessment completion
	  • Process risk assessment initiated
	  • Critical component dimensions and specifications definition
	• Design and Development Plan updates
	• Instructions for Use updates
	• Design History File updates
	• Engineering testing of prototype and conduct simulated use or clinical testing
	• Summative human factors study initiated
	• Design verification execution
	• Design Verification Review completion
	• Design validation execution
	• Design Validation Review completion
	• Design transfer completion
	• Design Transfer Review completion
	• Supply chain / logistics plan completion
	• **Complaint handling process definition**
	• Pharmacovigilance plan completion
		▪ A detailed plan to achieve the FIH CMC milestones is expected
		▪ Additionally, the plan should identify potential development risks to launch and risk mitigation strategies related to development timeline, costs, and resource allocation

* Items in **bold** font reflect suggested reporting guidelines for this stage gate

CMC DEVELOPMENT PLAN UPDATED (DRUGS)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

A detailed plan to address post-launch support – including technical issues during manufacturing and ongoing interactions with regulatory authorities.

CMC development plan updated.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ List of activities that will be conducted, that lead to achieving the Full-Scale Post-Launch Manufacturing Strategy Updated" milestone at PQ/LR stage gate	• Complete initial drug product characterization • Define cGMP manufacturing process • Complete GMP manufacturing for Ph 1 • Finalize DS characterization & analytical method development • Manufacture DS at kilo-scale • Complete DP characterization • Complete DP package characterization • Manufacture DP to support the Phase 2 clinical trial • Complete manufacturing process optimization • Complete GMP manufacturing for Ph 3 • Readiness for Tech Transfer • Complete technology transfer and validation of raw material, drug substance, and drug product analytical and functional release testing • Complete technology transfer and validation of drug substance & drug product manufacturing and packaging processes • Qualification of commercial-scale facilities • **Commercial launch strategy** • **QA/compliance activities** • **Ongoing CMC Support to ensure uninterrupted supply of high quality DP in all markets**	▪ A detailed plan to achieve the PQ/LR CMC milestones is expected ▪ Additionally, the Plan should identify potential development risks and risk mitigation strategies related to development timeline, costs and resource allocation ▪ CMC Development Plan should be final at the DTF gate review

* Items in **bold** font reflect suggested reporting guidelines for this stage gate

COGS UPDATED

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Business case for developing a deliverable product

Business Case, deliverability assessment, strategic demand forecast and COGS reports and cost effectiveness report

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE

▪ COGS	• The COGS analysis will include refined iterations of:
	  • Product price, volume, and revenue based on commercial scale production
	  • Variable and fixed costs (for all areas in COGS methodology)
	  • Licensing expenses and incomes
	  • Grants, loans and outstanding debts related to the product
	  • Related product sales
	  • Expected price, aligned with TPP & BMGF strategy
	  • Initial allocation and partner negotiation around shared and indirect costs
		▪ BMGF provides methodology

COST-EFFECTIVENESS ANALYSIS UPDATED

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Business case for developing a deliverable product

Business Case, deliverability assessment, strategic demand forecast and COGS reports and cost effectiveness report

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Cost-effectiveness analysis	The cost-effectiveness analysis will include refined iterations of: 1. Limitations of economic evaluations performed 2. Comparators and mean costs and effects of the product and the competitor 3. Cost and effects of the product on sub-populations 4. Groups that may be disproportionally impacted positively or negatively **Note: Additional inputs expected from Delivery team**	▪ BMGF provides methodology

COVERAGE AND FINANCIAL TRACKER

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Business case for developing a deliverable product

Business Case, deliverability assessment, strategic demand forecast and COGS reports and cost effectiveness report

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Coverage and Financial Tracker	The first iteration of the coverage and financial tracker should: 1. Develop target metrics for number of countries launched, coverage, average procurement price, and incremental costs to deliver *At PQ/LR these metrics should be refined.	▪ Draft target metrics

DELIVERY MILESTONES FOR DECISION TO FILE (1/3)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Business case for developing a deliverable product.

Business Case, deliverability assessment, strategic demand forecast and COGS reports and cost effectiveness report.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Delivery Plan	• The delivery plan will summarize: • Completed regulatory dossier ready for submission • Production/manufacturing supply chain and user targeting • Frequency and mode of delivery, e.g., special handling • Roll out plans for first-wave countries • Country decision support plans that verify capacity, resources, and new technologies for introduction • Considerations around global and country awareness of the intervention • Comparators with current standard of care • Patient access and perception of value and economics • Progress of government partnerships • Assessment of implementation capabilities and gaps • Provider-related issues, e.g., workflow and training • Coverage tracker metrics	▪ Summary report

DELIVERY MILESTONES FOR DECISION TO FILE (2/3)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Business case for developing a deliverable product.

Business Case, deliverability assessment, strategic demand forecast and COGS reports and cost effectiveness report.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Strategic demand Forecast	• The demand forecast will include refined iterations of : • Target countries for introduction • Target populations/sub-populations • Timing and speed of introduction specific to identified countries • Product accessibility and availability • Predicted coverage rate • Expected volumes and pricing • Sensitivity analysis based on key assumptions and drivers of forecast	▪ BMGF provides methodology
▪ COGS	• The COGS analysis will include refined iterations of: • Product price, volume, and revenue based on commercial scale production • Variable and fixed costs (for all areas in COGS methodology) • Licensing expenses and incomes • Grants, loans and outstanding debts related to the product • Related product sales • Expected price, aligned with TPP & BMGF strategy • Initial allocation and partner negotiation around shared and indirect costs	▪ BMGF provides methodology

DELIVERY MILESTONES FOR DECISION TO FILE (3/3)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Business case for developing a deliverable product.

Business Case, deliverability assessment, strategic demand forecast and COGS reports and cost effectiveness report.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Cost-effectiveness analysis	The cost-effectiveness analysis will include refined iterations of: 1. Limitations of economic evaluations performed 2. Comparators and mean costs and effects of the product and the competitor 3. Cost and effects of the product on sub-populations 4. Groups that may be disproportionally impacted positively or negatively Note: Additional inputs expected from Delivery team	▪ BMGF provides methodology
▪ Launch Budget Prediction	The refined launch budget prediction will provide: 1. A detailed and accurate estimation of the scale of launch support and budget for successful uptake	▪ Refined launch budget
▪ Coverage and Financial Tracker	The first iteration of the coverage and financial tracker should: 1. Develop target metrics for number of countries launched, coverage, average procurement price, and incremental costs to deliver *At PQ/LR these metrics should be refined.	▪ Draft target metrics

DELIVERY MILESTONES FOR DECISION TO FILE (1/3)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Business case for developing a deliverable product.

Business Case, deliverability assessment, strategic demand forecast and COGS reports and cost effectiveness report.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Delivery Plan	• The delivery plan will summarize: • Completed regulatory dossier ready for submission • Production/manufacturing supply chain and user targeting • Frequency and mode of delivery, e.g., special handling • Roll out plans for first-wave countries • Country decision support plans that verify capacity, resources, and new technologies for introduction • Considerations around global and country awareness of the intervention • Comparators with current standard of care • Patient access and perception of value and economics • Progress of government partnerships • Assessment of implementation capabilities and gaps • Provider-related issues, e.g., workflow and training • Coverage tracker metrics	▪ Summary report

DELIVERY MILESTONES FOR DECISION TO FILE (2/3)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Business case for developing a deliverable product.

Business Case, deliverability assessment, strategic demand forecast and COGS reports and cost effectiveness report.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Strategic demand Forecast	• The demand forecast will include refined iterations of : • Target countries for introduction • Target populations/sub-populations • Timing and speed of introduction specific to identified countries • Product accessibility and availability • Predicted coverage rate • Expected volumes and pricing • Sensitivity analysis based on key assumptions and drivers of forecast	▪ BMGF provides methodology
▪ COGS	• The COGS analysis will include refined iterations of: • Product price, volume, and revenue based on commercial scale production • Variable and fixed costs (for all areas in COGS methodology) • Licensing expenses and incomes • Grants, loans and outstanding debts related to the product • Related product sales • Expected price, aligned with TPP & BMGF strategy • Initial allocation and partner negotiation around shared and indirect costs	▪ BMGF provides methodology

DELIVERY MILESTONES FOR DECISION TO FILE (3/3)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Business case for developing a deliverable product.

Business Case, deliverability assessment, strategic demand forecast and COGS reports and cost effectiveness report.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Cost-effectiveness analysis	The cost-effectiveness analysis will include refined iterations of: 1. Limitations of economic evaluations performed 2. Comparators and mean costs and effects of the product and the competitor 3. Cost and effects of the product on sub-populations 4. Groups that may be disproportionally impacted positively or negatively Note: Additional inputs expected from Delivery team	▪ BMGF provides methodology
▪ Launch Budget Prediction	The refined launch budget prediction will provide: 1. A detailed and accurate estimation of the scale of launch support and budget for successful uptake	▪ Refined launch budget
▪ Coverage and Financial Tracker	The first iteration of the coverage and financial tracker should: 1. Develop target metrics for number of countries launched, coverage, average procurement price, and incremental costs to deliver *At PQ/LR these metrics should be refined.	▪ Draft target metrics

DESIGN HISTORY FILE CLOSED

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Complete the compilation of documentation that describes the design history of a finished medical device.

The DHF contains or references the records necessary to demonstrate that the design was developed in accordance with the approved design plan.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
• Design History File closed	a) Close Design History File when final data/information becomes available b) Changes made to product from CAPA need to be captured within the DHF	

DESIGN TRANSFER REVIEW

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

To ensure device design is translated into product specifications and begin to build-up product inventory for WHO PQ and launch.

Formalize procedures that ensure that the device design is correctly translated into product specifications and implement scale-up activities to build-up product inventory, manufactured at commercial scale, in preparation for WHO PQ and launch.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Design transfer completed	a) Analytical methods / specifications / acceptance criteria "locked" b) Clear demonstration of specifications that were set / achieved at laboratory scale are applicable at commercial scale c) Confirmation of suppliers being appropriately qualified if the packaging, API + excipients and / or device components will be sourced d) Complete documentation of Design Validation Master File, including protocols for Factory Acceptance Tests / Site Acceptance Tests and Installation Qualification / Operational Qualification e) Updated process risk assessments f) Updated control plans based on risk assessments	▪ Summary report containing key data / information to substantiate conclusions ▪ Illustrative data tables or figures may be reported in an appendix
• Design Transfer Review conducted	a) Conclusions and recommendations from the Design Transfer Review b) Control plans updated based on risk assessment and Design Transfer Review	

*Candidate progression is discussed at standing grantee update meetings with the investment team

Goals/ Definition

Development of a strategy to assess operational readiness for full-scale manufacturing launch, including a plan to engage internal CMC experts that have long-term experience with specifics of product and process development with commercial partners.

Operational readiness for full-scale manufacturing.

(*Full-Scale Post-Launch Manufacturing Strategy is initiated prior to the DTF gate review and is updated & reviewed again at PQ/LR gate review.)

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
Commercial launch strategy	a) Product expiry date proposal/strategy for regulatory submission b) Commercial launch strategy for each country market c) Finished product Warehouse qualified and operational d) Shipping validation complete	▪ Summary report
Quality Assurance/Compliance activities	a) Product registration b) Facility audit reports c) Audit observation compliance (CAPA, if required) d) Pre-approval inspection strategy, clear roles and responsibilities of partner and CRO/CMO	▪ Summary report
Plan for ongoing CMC Support to ensure uninterrupted supply of high quality DP in all markets	a) Establishment of bio-equivalence as appropriate (if the clinical development form and commercial form are not the same) b) Regular meetings with CMOs to monitor supply chain, review of quality incidents c) Ensure corrective actions such as improvements in systems/procedures, staff training d) Ensure timely support of technical support for manufacturing problems e) Evaluate process deviations/excursions during manufacturing that might affect quality f) Scientific evaluation of commercial product stability reports/problems g) Monitor and address changes in raw materials that affect manufacturing/product quality h) Timely submissions of periodic regulatory reports and regulatory agency interactions i) Assess impact of changes in Strategic Demand Forecast, determine whether alternate/additional manufacturing site or additional raw materials suppliers needed	▪ Summary report

GLOBAL ACCESS AGREEMENT UPDATED

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Global Access Strategy and Milestones in place.

Global Access is commitment from grantees and partners to making the products and information generated by foundation funding widely available at an affordable price, in sufficient volume, at a level of quality, and in a time frame that benefits the people we are trying to help.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Global Access Agreement with development, commercial and manufacturing partners available for stage gate approval	• Affirm commitment to a regulatory pathway that enables WHO prequalification • Ensure sufficient drug supply for use in developing countries • Secure affordable pricing for use by intended beneficiaries in developing countries	▪ Global Access commitments should be included in Grant Agreement
▪ Foundation – Grantee agreements in place that provide for Global Access	• Grant Agreement • Global Access Agreement • Price & Volume commitments • Volume Guarantee/Loan/PRI • Global Access License • Requirement to seek WHO PQ	
▪ Grantee – third party agreements in place that provide for Global Access	• Commercialization agreements • Procurement agreements • Sales & Distribution agreements • CMO agreements • Regulatory Approvals • Seeking/obtaining WHO PQ • Country approvals	

LAUNCH BUDGET PREDICTION UPDATED

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Business case for developing a deliverable product

Business Case, deliverability assessment, strategic demand forecast and COGS reports and cost effectiveness report

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Launch Budget Prediction	The refined launch budget prediction will provide: 1. A detailed and accurate estimation of the scale of launch support and budget for successful uptake	▪ Refined launch budget

PHASE 3 ENDPOINTS MET

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Safety, efficacy, and desired outcomes in humans demonstrated in pivotal trial.

Safety, efficacy, and desired outcomes in humans (full analysis) demonstrated.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Safety (includes clinical and laboratory abnormalities) profile of candidate aligns with TPP	Satisfactory safety profile using validated clinical endpoint assays and adequate statistical analyses: a) Safety signal detection (e.g., adverse events (AEs) which may includeserious adverse events (SAEs)) b) Fully characterized drug-drug interactions c) Management of any adverse events (reporting of the events to the applicableethical committees and regulatory agencies)	▪ Summary of Phase 3 clinical trial data
▪ Efficacy profile of candidate aligns with TPP	Clinical efficacy demonstrated using validated clinical endpoint assays and adequate statistical analyses: 1) Sufficient efficacy duration to achieve impact 2) Superiority ornon-inferiority datain comparative studies against licensed drug (or treatment) control (if applicable)	▪ Summary of Phase 3 clinical trial data
▪ Other TPP characteristics met	Assessment of whethercandidatemeets target product profile	▪ Use cTPP template

PRE-LICENSURE MEETING SCHEDULED*

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Gain concurrence with Regulatory Authority on licensure

Pre-licensure meeting(s) in country of manufacture conducted.
(*Specific communication requirements of National Regulatory Authorities (NRA) should be identified upon initiation of the Regulatory Strategy Plan)

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Requirements for pre-licensure meeting(s) in country of manufacture completed; endorsed, submitted to NRA(s)	a) Safety and efficacy data from all clinical trials b) Product release specifications (including pre-approval inspection of manufacturing facilities) c) Stability data to support expiration dating d) Claims and indication statement in the product label e) If applicable, agreement on deferral (or waiver) of pediatric studies f) Plans for any post-approval clinical studies and pharmacovigilance plan g) Information on transition from clinical to commercial-scale manufacture (i.e., establishing comparability of the Phase 3 and commercial products) h) Plans for organizing the content of the application and the submission type (paper vs. electronic) i) Determine if any type of advisory committee meeting will be necessary (if applicable) j) Determine schedule/route of communications with NRA during review process	▪ End of Pre-licensure briefing package
▪ Post-meeting debrief and development strategy adjustment (if required) completed	a) Minutes of meeting prepared by sponsor. NRA minutes obtained (if possible). Review of decisions and recommendations made at the meeting. b) Action plan to address highlighted development issues (if any) prior to filing of application	▪ Regulatory responses to questions

REGULATORY STRATEGY AND PLAN UPDATED

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Regulatory path and plan in place.

Plan for proposed regulatory path through life-cycle of the product
(Regulatory Strategy Plan in initiated prior to the FIH gate review and is updated & reviewed during development through to the DTF gate review)

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Proposed regulatory path through life-cycle of product defined, including clinical development, licensure, WHO PQ (if needed), and post-authorization safety surveillance and further product development ▪ Include any specific plans to use alternative development pathways (conditional, accelerated, breakthrough) or registration processes (article 58, tropical voucher, orphan)	**a) Prioritized list of countries where the drug is intended to be introduced** **b) Understanding of country-specific regulatory requirements** • **Type of submissions (original, supplement/variation, line extension, etc)** • **Significant / unique requirements** • **Required HA communications and timing** **c) Plans for NRA engagement during development to gain feedback and agreement with development and filing strategy** **d) Key regulatory risks and risk mitigation plans** **e) Plan to ensure proposed indication and labeling aligns with TPP and donor/utilization requirements** f) Plan for approval and protocol review for clinical trial starts in target countries g) Plan to handle monitoring and reporting of adverse events and safety issues during clinical trials and post-authorizations **h) WHO PQ applicability/programmatic suitability, plan to pursue WHO PQ (if applicable)** i) **Plans for WHO PQ engagement by end of phase 2 (if applicable)**	▪ Updated throughout life-cycle of product reflecting new data and priorities as they develop ▪ Required at each gate: Detailed plan with timeline and resources for the next phase of development, and high-level/draft plan focusing on risk identification and mitigation for all subsequent phases of development

* Items in **bold** font reflect suggested reporting guidelines for this stage gate

RUN CLINICAL PROGRAM (1/7)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Track clinical trial start date.

Track the dosing of the first subject enrols thereby indicating the beginning of the clinical trial.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Track first dosing event for a patient recruited to the Phase 3 clinical trial	a) Conduct recruitment analysis and compare study starts to the clinical plan b) Inform impact on other planned downstream activities in the case of study start delays	▪ Notification of date first subject dosed and any delay, if incurred

RUN CLINICAL PROGRAM (2/7)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Track that enrolment in the clinical trial is proceeding according to plan.

Track the progress and feasibility of Phase 3 clinical trials.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
• Track recruitment and budget by comparing actual patient enrollment to previously established benchmarks at 25% of the projected recruitment period	a) Conduct recruitment analysis and report number of patients recruited and budget within 25% of the projected recruitment period b) If suboptimal recruitment is identified, submit an analysis of recruitment barriers and a corrective recruitment plan with revised budget and timeline c) If recruitment levels are below minimum acceptable levels: evaluate feasibility to complete study within acceptable budget or timeframe and submit corrective recruitment plan	▪ Notification of milestone achievement, any delay, mitigations and revised timeline

RUN CLINICAL PROGRAM (3/7)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Check that data quality is on track to meet target clinical study report date.

Monitor data cleaning process to expedite database lock, data analysis, and data submission.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Initiate data cleaning process as data becomes available to allow access to high integrity and quality data and expedite data analysis and submission *NOTE: Data cleaning process and plan should be clearly defined at the beginning of the study. Readiness for database lock should be considered at patient level and entire data base level.*	a) Streamlined data cleaning process to expedite clinical data analysis and submission b) Provide estimated time to database lock, data analysis, and data submission c) Report SAEs and any other issues	▪ Notification of milestone achievement, any delay, mitigations and revised timeline

RUN CLINICAL PROGRAM (4/7)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Obtain an early read-out on the Phase 3 (if applicable) that may enable acceleration of regulatory submission.

Phase 3 interim analysis completed (preferably by independent committees).

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Safety assessment completed	a) Rate of severe adverse events (SAEs)	▪ Interim clinical study report
▪ Efficacy assessment completed	a) Statistically significant efficacy	▪ As above
▪ Futility assessment (inability of trial to meet its objectives) completed	a) Futility of trial effects (unlikely to achieve statistical significant efficacy) b) Operational futility (i.e., poor execution, lack of adequate resources, low adherence, poor quality of data)	▪ As above
▪ Clinical trial strategy adjustment (if needed)	a) Sample size re-adjustment b) Additional testing requirements	▪ Updated IPDP
▪ TPP achievement assessed	a) Probability assessment of whether candidate will meet target product profile	▪ Use cTPP template

RUN CLINICAL PROGRAM (5/7)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Track Clinical Trial end date.

Track the date for the last subject to complete the trial thereby indicating the end of the clinical trial.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Track last patient to complete the Phase 3 clinical trial	a) Conduct recruitment analysis and compare study duration to the clinical plan b) Inform impact on other planned downstream activities in the case of study completion delays	▪ Notification of date last subject last visit and any delay, if incurred

RUN CLINICAL PROGRAM (6/7)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Leading indicator of availability of study analyses.

Track the time of database lock that informs the lag between the last subject dosed and the availability of study analyses.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Action taken to prevent further changes to the clinical trial database	a) Database review and query resolution completed b) All pharmacokinetic, laboratory safety data and CRF data transferred to Data Management c) Database review and quality checks complete, data queries identified d) Query resolution completed	▪ Notification of milestone achievement, any delay, mitigations and revised timeline

RUN CLINICAL PROGRAM (7/7)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Track availability of clinical trial data for decision making.

Track the availability of top line results that enable real-time discussions of clinical trial data analysis and earlier investment decisions.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Statistical analyses using preliminary or final data are completed	a) Pharmacokinetic and pharmacodynamics (PK/PD) analyses of data completed b) Comparison of the observed results to the minimum criteria in the candidate TPP c) Working data sets delivered d) Tables, listings, figures produced to support topline report writing	▪ Notification of milestone achievement, any delay, mitigations and revised timeline

RUN CLINICL PROGRAM PHASE 3 (1/7)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Track clinical trial start date.

Track the dosing of the first subject enrolled thereby indicating the beginning of the clinical trial.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Track first dosing event for a patient recruited to the Phase 3 clinical trial	a) Conduct recruitment analysis and compare study starts to the clinical plan b) Inform impact on other planned downstream activities in the case of study start delays	▪ Notification of date first subject dosed and any delay, if incurred

RUN CLINICL PROGRAM PHASE 3 (2/7)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Track that enrolment in the clinical trial is proceeding according to plan.

Track the progress and feasibility of Phase 3 clinical trials.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
• Track recruitment and budget by comparing actual patient enrollment to previously established benchmarks at 25% of the projected recruitment period	a) Conduct recruitment analysis and report number of patients recruited and budget within 25% of the projected recruitment period b) If suboptimal recruitment is identified, submit an analysis of recruitment barriers and a corrective recruitment plan with revised budget and timeline c) If recruitment levels are below minimum acceptable levels: evaluate feasibility to complete study within acceptable budget or timeframe and submit corrective recruitment plan	▪ Notification of milestone achievement, any delay, mitigations and revised timeline

RUN CLINICL PROGRAM PHASE 3 (3/7)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Check that data quality is on track to meet target clinical study report date.

Monitor data cleaning process to expedite database lock, data analysis, and data submission.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Initiate data cleaning process as data becomes available to allow access to high integrity and quality data and expedite data analysis and submission *NOTE: Data cleaning process and plan should be clearly defined at the beginning of the study. Readiness for database lock should be considered at patient level and entire data base level.*	a) Streamlined data cleaning process to expedite clinical data analysis and submission b) Provide estimated time to database lock, data analysis, and data submission c) Report SAEs and any other issues	▪ Notification of milestone achievement, any delay, mitigations and revised timeline

RUN CLINICL PROGRAM PHASE 3 (4/7)

GLOBAL DRUG DEVELOPMENT

Goals / Definition

Obtain an early read-out on the Phase 3 (if applicable) that may enable acceleration of regulatory submission.

Phase 3 interim analysis completed (preferably by independent committees).

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Safety assessment completed	a) Rate of severe adverse events (SAEs)	▪ Interim clinical study report
▪ Efficacy assessment completed	a) Statistically significant efficacy	▪ As above
▪ Futility assessment (inability of trial to meet its objectives) completed	a) Futility of trial effects (unlikely to achieve statistical significant efficacy) b) Operational futility (i.e., poor execution, lack of adequate resources, low adherence, poor quality of data)	▪ As above
▪ Clinical trial strategy adjustment (if needed)	a) Sample size re-adjustment b) Additional testing requirements	▪ Updated IPDP
▪ TPP achievement assessed	a) Probability assessment of whether candidate will meet target product profile	▪ Use cTPP template

RUN CLINICL PROGRAM PHASE 3 (5/7)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Track Clinical Trial end date.

Track the date for the last subject to complete the trial thereby indicating the end of the clinical trial.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Track last patient to complete the Phase 3 clinical trial	a) Conduct recruitment analysis and compare study duration to the clinical plan b) Inform impact on other planned downstream activities in the case of study completion delays	▪ Notification of date last subject last visit and any delay, if incurred

RUN CLINICL PROGRAM PHASE 3 (6/7)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Leading indicator of availability of study analyses.

Track the time of database lock that informs the lag between the last subject dosed and the availability of study analyses.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Action taken to prevent further changes to the clinical trial database	a) Database review and query resolution completed b) All pharmacokinetic, laboratory safety data and CRF data transferred to Data Management c) Database review and quality checks complete, data queries identified d) Query resolution completed	▪ Notification of milestone achievement, any delay, mitigations and revised timeline

RUN CLINICL PROGRAM PHASE 3 (7/7)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Track availability of clinical trial data for decision making.

Track the availability of top line results that enable real-time discussions of clinical trial data analysis and earlier investment decisions.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Statistical analyses using preliminary or final data are completed	a) Pharmacokinetic and pharmacodynamics (PK/PD) analyses of data completed b) Comparison of the observed results to the minimum criteria in the candidate TPP c) Working data sets delivered d) Tables, listings, figures produced to support topline report writing	▪ Notification of milestone achievement, any delay, mitigations and revised timeline

STRATEGIC DEMAND FORECAST UPDATED

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Business case for developing a deliverable product

Business Case, deliverability assessment, strategic demand forecast and COGS reports and cost effectiveness report

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE

▪ Strategic demand Forecast	• The demand forecast will include refined iterations of:
	  • Target countries for introduction
	  • Target populations/sub-populations
	  • Timing and speed of introduction specific to identified countries
	  • Product accessibility and availability
	  • Predicted coverage rate
	  • Expected volumes and pricing
	  • Sensitivity analysis based on key assumptions and drivers of forecast
		▪ BMGF provides methodology

SUPPLY CHAIN / LOGISTICS PLAN IN PLACE

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Develop a plan for the supply chain and associated logistics to ensure product can be distributed to the appropriate locations for launch.

Turn and move all raw materials to the final combination products and then transfer to customers/users.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Supply chain / logistics plan in place	a) Sufficient inventory build up based on demand forecast and management of on-going supply chain b) Transportation design validation reports developed from commercially representative lots c) Verification that incoming, in-process, and final commercial packaging specifications and labeling are in place d) Definition and implementation of tracking capabilities with distributors e) Confirmation of import and export practices meeting local laws and regulations f) Establishment of mechanisms for recalls g) Commercial packs designed and ready for regulatory submission at risk of potential changes by regulators just prior to approval	

TECH TRANSFER (DS, ANALYTICAL, DP & PACKAGING), VALIDATION COMPLETED (1/2)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Completion of launch-related transition of manufacturing processes to full-scale/ commercial facilities to ensure uninterrupted supply of high quality product upon regulatory approval.

Drug manufacturing process technology transferred and validated.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
Technology transfer and validation of raw material, drug substance, and drug product analytical and functional release testing completed	a) SOP-driven tech transfer and validation protocols b) Validation package including, at a minimum, the following data for each method used for analytical and functional release testing (in line/at line/off line): • Specificity • Sensitivity • Variability/reproducibility	▪ Summary report
Technology transfer and validation of drug substance & drug product manufacturing and packaging processes completed	a) SOP-driven tech transfer and validation protocols b) Overview of manufacturing process, siting, equipment, quality control tools, etc. c) Safety and ecological assessment of drug substance and drug product manufacturing processes d) Validation package including, at a minimum: • Batch campaign summary • Final operating conditions • Control strategy for on-going production e) Three validation batches on stability	▪ Summary report

TECH TRANSFER (DS, ANALYTICAL, DP & PACKAGING), VALIDATION COMPLETED (2/2)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Completion of launch-related transition of manufacturing processes to full-scale/ commercial facilities to ensure uninterrupted supply of high quality product upon regulatory approval.

Drug manufacturing process technology transferred and validated.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
Qualification of commercial-scale facilities completed	a) Site master plan (e.g., facility design, maintenance, equipment, calibration schedule, staff training, etc.) b) cGMP certification c) Audits by FDA/NRAs and client d) Commercial-scale batch records e) Change control strategy f) Notice of Event/Deviation reporting mechanism g) Action plan for response to regulatory authority inspections, audits, questions/interactions	▪ Summary report
Documentation and Reports	a) On-going stability program b) Stability reports c) Process Qualification reports d) Master batch record for commercial manufacturing finalized e) Vendor qualification reports f) SOPs for commercial manufacturing, testing, storage and distribution g) Stability in DS and DP primary containers h) Labeling study report i) Shipping stability study report	▪ Summary report

TECH TRANSFER (DS, ANALYTICAL, DP & PACKAGING), VALIDATION COMPLETED (1/2)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Completion of launch-related transition of manufacturing processes to full-scale/ commercial facilities to ensure uninterrupted supply of high quality product upon regulatory approval.

Drug manufacturing process technology transferred and validated.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Technology transfer and validation of raw material, drug substance, and drug product analytical and functional release testing completed	a) SOP-driven tech transfer and validation protocols b) Validation package including, at a minimum, the following data for each method used for analytical and functional release testing (in line/at line/off line): • Specificity • Sensitivity • Variability/reproducibility	▪ Summary report
▪ Technology transfer and validation of drug substance & drug product manufacturing and packaging processes completed	a) SOP-driven tech transfer and validation protocols b) Overview of manufacturing process, siting, equipment, quality control tools, etc. c) Safety and ecological assessment of drug substance and drug product manufacturing processes d) Validation package including, at a minimum: • Batch campaign summary • Final operating conditions • Control strategy for on-going production e) Three validation batches on stability	▪ Summary report

*Candidate progression is discussed at standing grantee update meetings with the investment team

TECH TRANSFER (DS, ANALYTICAL, DP & PACKAGING), VALIDATION COMPLETED (2/2)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Completion of launch-related transition of manufacturing processes to full-scale/ commercial facilities to ensure uninterrupted supply of high quality product upon regulatory approval.

Drug manufacturing process technology transferred and validated.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Qualification of commercial-scale facilities completed	a) Site master plan (e.g., facility design, maintenance, equipment, calibration schedule, staff training, etc.) b) cGMP certification c) Audits by FDA/NRAs and client d) Commercial-scale batch records e) Change control strategy f) Notice of Event/Deviation reporting mechanism g) Action plan for response to regulatory authority inspections, audits, questions/interactions	▪ Summary report
▪ Documentation and Reports	a) On-going stability program b) Stability reports c) Process Qualification reports d) Master batch record for commercial manufacturing finalized e) Vendor qualification reports f) SOPs for commercial manufacturing, testing, storage and distribution g) Stability in DS and DP primary containers h) Labeling study report i) Shipping stability study report	▪ Summary report

*Candidate progression is discussed at standing grantee update meetings with the investment team

UPDATED CANDIDATE TTP

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Candidate Target Product Profile Agreed

The Candidate Target Product Profile (cTTP) describes the desired attributes of the product and are consistent with mechanism of action and preclinical data.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ cTPP developed and agreed	• Indication, use case, and target population • Global health impact • Proposed mechanism of action • Manufacturability • Formulation, dosing, and stability • Route of administration • Shelf-life and storage • Cost and delivery considerations • Product registration strategy • Alignment with partner organizations	▪ Use cTPP template – should reflect the desired Intervention TPP (iTPP)

50% C (50% COVERAGE ACHIEVED)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Date when anticipate achieving 50% of the program strategy team's coverage goal for the overall product class (see below) – i.e., fi the goal for rotavirus vaccines is 80% coverage in Gavi countries, then year X is when coverage is expected to achieve the half-way point (40% coverall in all, or 80% in half of Gavi countries); if the target is 20m male circumcisions in target geographies, then year Y when coverage is expected to achieve the half-way point (10m).

Product class is defined as the general category that is the next order up from the candidate or product name. This is likely to align with how coverage tracked for a health intervention. Examples are rotavirus vaccine, HIV first-line drug, TB molecular diagnostic, etc. Please specify the product class in the "Target Coverage/Market Share Description" field.

GNG (GLOBAL NORMATIVE GUIDANCE)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Date when critical normative guidance (country adoption into national guidelines if in a single focal country, WHO policy guidance, SAGE recommendation, other) is announced publicly.

LFC (LAUNCH IN FIRST COUNTRY)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Date when country or large-scale private agency formally incorporate product into system planning/financing (i.e., not temporary pilot, demonstration or operational research)

TMS (TARGET MARKET SHARE ACHIEVED)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Date when anticipate this specific product will achieve the target market share for the overall product class – i.e., Year X when Gene X-pert will represent 25% market share of all TB molecular diagnostics.

This should be informed by a demand forecast and initially should mirror the assumptions made for impact modeling and should be refine over time with more concrete demand forecasts. Please leave blank if the team is agnostic as to coverage of the specific product and is more interested in overall coverage of the product class or if this is the only product class or if the team has not yet thought through these questions.

BUSINESS CASE

GLOBAL DRUG DEVELOPMENT

Goals/Definitions

Business case for developing a deliverable product

Business Case, deliverability assessment, strategic demand forecast and COGS reports and cost effectiveness report

CRITERIA	SAMPLE CONTENT REQUIREMENT/ MILESTONE EXPECTATIONS	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE

▪ Business Case	• Business case provides overview of product candidate's strategic value and market viability, including:
	  • Value proposition against foundation's disease strategy and other interventions in market
	  • Estimate of overall costs to launch and drive uptake
	  • Summary of market understanding (e.g., size, segments, user needs, etc.)
		▪ Provide key assumptions and rationale for business case

CANDIDATE TARGET PRODUCT PROFILE EXPECTATIONS

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Candidate Target Product Profile Agreed.

The Candidate Target Product Profile (cTPP) describes the desired attributes of the product and are consistent with mechanism of action and preclinical data.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ cTPP developed and agreed	• Drug need, use case, market, and impact on global health • Product characteristics required to show benefit, such as efficacy, safety, and duration of treatment outlined • Primary endpoints and secondary endpoints • Alignment with partner organizations	▪ Use cTPP template – should reflect the desired Intervention TPP (iTPP)

CLINICAL DEVELOPMENT PLAN IN PLACE

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Detailed plan for Phase 1 and high level plan for Phase 2 and 3 in place.

Clinical Development Plan initiated.

(*Clinical Development Plan is initiated to the FIH gate review and is updated & reviewed during development through to the DTF gate review)

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
• Clinical development plan initiated	a) Overview of planned clinical activities: • Study phase, objectives / research rationale • Duration of the studies, number of subjects, recruitment criteria (e.g.,. study arms, patient cohorts, comparators for non-inferiority trials, power calculations etc.) • Dosing & dosing modeling strategies • Detailed rationale for Phase 1 dose range, and target clinical exposures • Toxicology and toxic kinetic results to support doses and dosing duration in Phase 2 • Drug combination assessment & plan • Toxicology plan to support Phase 2 b) Clinical partners, proposed target countries, and study sites (based on criteria including clinical expertise, sustainability, site capacity, and disease incidence / epidemiology studies, etc.) c) Definition of clinical endpoints (primary & secondary), methodology (clinical endpoint assays, data collection plan, statistical methods, etc.), adverse event reporting, stopping rules, etc. d) Monitoring, data management, and biostatistics strategies e) Post-marketed product surveillance / Phase 4 trial strategy f) Mass product administration considerations (e.g., trial design, safety requirements, etc.) g) Off-label use considerations h) Trial size considerations for diseases with limited incidence rates i) Potential risks and mitigation strategies j) Timelines and budgets for clinical development	• Detailed plan with timeline for Phase 1 • High-level / draft plan for Phase 2 and Phase 3 risk identification and mitigation • Plans should reflect approaches to accelerate decision making (e.g., adaptive designs, real-time data analysis of clinical trials etc.) • Phase 2 plan is modified during Phase 1 trial as Phase 1 data become available • Clinical development plan extends beyond DTF to accommodate the time needed to report Phase 3 results and also cover additional plans for pediatric studies and post-market surveillance

CMC DEVELOPMENT PLAN UPDATED (CP/ADDS) (1/2)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

A detailed plan for completing the initial design and characterization of the combination product at EP1 stage gate.

CMC development plan updated.

CRITERIA	SAMPLE CONTENT REQUIREMENT		GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ List of activities that will be conducted, that lead to achieving Product Definition and Planning milestone at EP1 stage gate	Plans to complete the following bolded items by the next stage gate: • User capabilities and preferences assessment • Ethnographic studies completion • Hazard identification initiation • Concept assessment completion • Design and development plan initiation • Instructions for Use drafts • Human Factors Study Plan • Application risk assessment completion • Design History File initiation • Design Input Review completion • High-level Project Plan and definition of critical product attributes (if prototype available) • Preliminary device prototype generation • **Design Output Review completion** • **Formative human factors study completion** • **Design risk assessment completion** • **Process risk assessment initiated** • **Critical component dimensions and specifications definition** • **Design and Development Plan updates** • **Instructions for Use updates** • **Design History File updates**	• **Engineering testing of prototype and conduct simulated use or clinical testing** • Summative human factors study initiated • Design verification execution • Design Verification Review completion • Design validation execution • Design Validation Review completion • Design transfer completion • Design Transfer Review completion • Supply chain / logistics plan completion • Complaint handling process definition • Pharmacovigilance plan completion	▪ A detailed plan to achieve the FIH CMC milestones is expected ▪ Additionally, the plan should identify potential development risks to launch and risk mitigation strategies related to development timeline, costs, and resource allocation

CMC DEVELOPMENT PLAN UPDATED (CP/ADDS) (2/2)

GLOBAL DRUG DEVELOPMENT

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Instructions for Use drafted	a) Evaluation of appropriate labeling / packaging requirements for the combination product when they are single-entity (e.g., pre-filled syringes, vaginal rings), or physically combined and packaged together (e.g., drug vial with syringe with or without vial adapter) or for separate "cross-labeled" products (e.g., vial adaptor, finger flange with back stop) b) Confirmation that Instructions for Use addresses any use errors or residual user risk related to product safety and efficacy, which cannot be adequately mitigated by product re-design	▪ Summary report containing key data / information or information to substantiate conclusions ▪ Illustrative data tables or figures may be reported in an appendix
▪ Application risk assessment completed	a) Identification of potential use problems not apparent from analytical measurements, e.g., the demands associated with use exceed user capabilities b) Initial design review to evaluate adequacy of the design to fulfill intended application c) Appropriate risk mitigation strategies and definition of what residual risk is acceptable	
▪ High-level Project Plan created and critical product attributes (CPAs) defined (if prototype available)	a) Essential processes and equipment required for product development b) Development of prototype tooling and test equipment c) Review of product development plan to understand drug-device interface and alignment between drug stability and device shelf-life attributes. Determine if there are potential interactions between drug and device that would impact the performance/efficacy of the functioning of the device as well as the safety and efficacy of the drug action d) Initiate CMO / suppliers selection process	• Summary report containing key data / information or information to substantiate conclusions ▪ Illustrative data tables or figures may be reported in an appendix
▪ Preliminary device prototype generated	a) Development of early-stage device prototype for Formative Human Factor Studies	
▪ Review TPP	a) Review TPP developed and determine if modifications are necessary	

* Items in **bold** font reflect suggested reporting guidelines for this stage gate

CMC DEVELOPMENT PLAN UPDATED (DRUGS)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

To describe a detailed plan to scale-up manufacturing to provide larger amounts (kilo scale) of clinical trial materials (drug substance and drug product) that will be required for Phase 2 clinical trials.

CMC development plan updated.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ List of activities that will be conducted, that lead to achieving the "DS/DP Characterized at Kilo-Scale" milestone at EP1 stage gate	• Complete initial drug product characterization • Define cGMP manufacturing process • Complete GMP manufacturing for Ph 1 • Finalize DS characterization & analytical method development • Manufacture DS at kilo-scale • Complete DP characterization • Complete DP package characterization • Manufacture DP to support the Phase 2 clinical trial • Manufacturing process optimization • GMP manufacturing for Ph 3 • Readiness for Tech Transfer • Technology transfer and validation of raw material, drug substance, and drug product analytical and functional release testing • Technology transfer and validation of drug substance & drug product manufacturing and packaging processes • Qualification of commercial-scale facilities • Commercial launch strategy • QA/compliance activities • Ongoing CMC Support to ensure uninterrupted supply of high quality DP in all markets	▪ A detailed plan to achieve the EP1 CMC milestones is expected ▪ Additionally, the Plan should identify potential development risks to PQ, and risk mitigation strategies related to development timeline, costs and resource allocation

COGS

GLOBAL DRUG DEVELOPMENT

Goals/Definitions

Business case for developing a deliverable product

Business Case, deliverability assessment, strategic demand forecast and COGS reports and cost effectiveness report

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ COGS	• Methodology to be used to build up COGS over the course of product development • During FIH, an initial aspirational COGS should be set to drive TPP and goals for projected costs related to the product	▪ BMGF provides methodology

COST-EFFECTIVENESS ANALYSIS

GLOBAL DRUG DEVELOPMENT

Goals/Definitions

Business case for developing a deliverable product

Business Case, deliverability assessment, strategic demand forecast and COGS reports and cost effectiveness report

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Cost-Effectiveness Analysis	• Methodology to be used to assess drivers of health and economic outcomes and interventions/product candidates • BMGF provides a methodology grantees may use for cost-effectiveness analysis • Cost-effectiveness methods should align with to the BMGF valuation model (in Integrated Portfolio Management tool)	▪ BMGF provides methodology

DELIVERABILITY ASSESSMENT

GLOBAL DRUG DEVELOPMENT

Goals/Definitions

Business case for developing a deliverable product

Business Case, deliverability assessment, strategic demand forecast and COGS reports and cost effectiveness report

CRITERIA	SAMPLE CONTENT REQUIREMENT/ MILESTONE EXPECTATIONS	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Deliverability Assessment	• A deliverability assessment will provide a high-level assessment of risks and opportunities for: • Improvement relative to standard of care • Considerations around the global and country awareness of the intervention, possibility of financing, • Global policy and regulatory pathway • Supply chain and user targeting • Frequency and mode of delivery and any special handling required • Novelty relative to existing products • Manufacturing considerations • Provider-related issues including workflow and training (ex: maintenance and calibration) • Patient access, perception of value and economics • Disease risk awareness in population	▪ Summary report

DELIVERY DECISION TO ENTER PHASE 1 TRIALS (1/2)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Business case for developing a deliverable product.

Business Case, deliverability assessment, strategic demand forecast and COGS reports and cost effectiveness report.

CRITERIA	SAMPLE CONTENT REQUIREMENT/ MILESTONE EXPECTATIONS	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE

▪ Business Case	• Business case provides overview of product candidate's strategic value and market viability, including:
	  • Value proposition against foundation's disease strategy and other interventions in market
	  • Estimate of overall costs to launch and drive uptake
	  • Summary of market understanding (e.g., size, segments, user needs, etc.)
		▪ Provide key assumptions and rationale for business case

▪ Deliverability Assessment	• A deliverability assessment will provide a high-level assessment of risks and opportunities for:
	  • Improvement relative to standard of care
	  • Considerations around the global and country awareness of the intervention, possibility of financing,
	  • Global policy and regulatory pathway
	  • Supply chain and user targeting
	  • Frequency and mode of delivery and any special handling required
	  • Novelty relative to existing products
	  • Manufacturing considerations
	  • Provider-related issues including workflow and training (ex: maintenance and calibration)
	  • Patient access, perception of value and economics
	  • Disease risk awareness in population
		▪ Summary report

DELIVERY DECISION TO ENTER PHASE 1 TRIALS (2/2)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Business case for developing a deliverable product.

Business Case, deliverability assessment, strategic demand forecast and COGS reports and cost effectiveness report.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Strategic Demand Forecast	• Methodology to be used to assess potential demand adjusted for product availability, country introduction decisions, uptake timing (without any supply or financing constraints) • BMGF provides a methodology grantees may use for demand forecasting • Demand forecast methods should align with to the BMGF valuation model (in Integrated Portfolio Management tool)	▪ BMGF provides methodology
▪ COGS	• Methodology to be used to build up COGS over the course of product development • During FIH, an initial aspirational COGS should be set to drive TPP and goals for projected costs related to the product	▪ BMGF provides methodology
▪ Cost-Effectiveness Analysis	• Methodology to be used to assess drivers of health and economic outcomes and interventions/product candidates • BMGF provides a methodology grantees may use for cost-effectiveness analysis • Cost-effectiveness methods should align with to the BMGF valuation model (in Integrated Portfolio Management tool)	▪ BMGF provides methodology

DELIVERY DECISION TO ENTER PHASE 1 TRIALS (1/2)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Business case for developing a deliverable product.

Business Case, deliverability assessment, strategic demand forecast and COGS reports and cost effectiveness report.

CRITERIA	SAMPLE CONTENT REQUIREMENT/ MILESTONE EXPECTATIONS	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE

▪ Business Case	• Business case provides overview of product candidate's strategic value and market viability, including:
	  • Value proposition against foundation's disease strategy and other interventions in market
	  • Estimate of overall costs to launch and drive uptake
	  • Summary of market understanding (e.g., size, segments, user needs, etc.)
		▪ Provide key assumptions and rationale for business case

▪ Deliverability Assessment	• A deliverability assessment will provide a high-level assessment of risks and opportunities for:
	  • Improvement relative to standard of care
	  • Considerations around the global and country awareness of the intervention, possibility of financing,
	  • Global policy and regulatory pathway
	  • Supply chain and user targeting
	  • Frequency and mode of delivery and any special handling required
	  • Novelty relative to existing products
	  • Manufacturing considerations
	  • Provider-related issues including workflow and training (ex: maintenance and calibration)
	  • Patient access, perception of value and economics
	  • Disease risk awareness in population
		▪ Summary report

DELIVERY DECISION TO ENTER PHASE 1 TRIALS (1/2)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Business case for developing a deliverable product.

Business Case, deliverability assessment, strategic demand forecast and COGS reports and cost effectiveness report.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Strategic Demand Forecast	• Methodology to be used to assess potential demand adjusted for product availability, country introduction decisions, uptake timing (without any supply or financing constraints) • BMGF provides a methodology grantees may use for demand forecasting • Demand forecast methods should align with to the BMGF valuation model (in Integrated Portfolio Management tool)	▪ BMGF provides methodology
▪ COGS	• Methodology to be used to build up COGS over the course of product development • During FIH, an initial aspirational COGS should be set to drive TPP and goals for projected costs related to the product	▪ BMGF provides methodology
▪ Cost-Effectiveness Analysis	• Methodology to be used to assess drivers of health and economic outcomes and interventions/product candidates • BMGF provides a methodology grantees may use for cost-effectiveness analysis • Cost-effectiveness methods should align with to the BMGF valuation model (in Integrated Portfolio Management tool)	▪ BMGF provides methodology

DESIGN HISTORY FILE INITIATED

GLOBAL DRUG DEVELOPMENT

Goal / Definition

To initiate the compilation of documentation that describes the design history of a finished medical device

The DHF contains or references the records necessary to demonstrate that the design was developed in accordance with the approved design plan.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
• Design History File initiated	a) Design History File to document history of the device design and the design controls elements b) Design Input Requirements	

DESIGN INPUT REVIEW

GLOBAL DRUG DEVELOPMENT

Goal / Definition

Conduct a Design Input Review for the initial requirements that describe the medical devices to be produced.

Design review is a documented, comprehensive, systematic examination of a design to evaluate the adequacy of the design requirements, to evaluate the capability of the design to meet these requirements, and to identify problems.

In general, formal design reviews are intended to:

- **Provide a systematic assessment of design results, including the device design and the associated designs for manufacturing (DFM) and support processes.**
- **Assess project progress; and/or**
- **Proved confirmation that the project is ready to move on the next stage of development**

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
• Design Input Review conducted	a) Conclusions and recommendations from the Design Input Review b) Control plans updated based on risk assessment and Design Input Review	▪ Summary report containing key data / information or information to substantiate conclusions ▪ Illustrative data tables or figures may be reported in an appendix

DEVICE DESIGN AND DEVELOPMENT PLAN INITIATED

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Initiate the development of the Design and Development Plan.

Establish and maintain plans that: (1) Describe or reference design and development activities. (2) Define responsibility for implementation. (3) Identify or describe interfaces with different groups or activities. (4) Review, document, update and approve plans as design and development evolves.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Design and Development Plan initiated	a) Drug-device product Critical Quality Attributes (CQAs) ** and Critical Material Attributes (CMAs), as per the TPP b) Initiation of design control activities including associated documentations c) Initial quality plan d) Technical feasibility assessment e) Alignment on roles and responsibilities for different parties involved (i.e. specification developer, conduct of investigations, IP, publication policy etc.)	

GLOBAL ACCESS AGREEMENT EXPECTATION

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Global Access Strategy and Milestone in place.

Global Access is commitment from grantees and partners to making the products and information generated by foundation funding widely available at an affordable price, in sufficient volume, at a level of quality, and in a time frame that benefits the people we are trying to help.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Initial agreement on commitments to underpin the Global Access Agreement and future commercial / manufacturing partner selection	• Affirm commitment to a regulatory pathway that enables WHO prequalification • Ensure sufficient drug supply for use in developing countries • Secure affordable pricing for use by intended beneficiaries in developing countries	▪ Global Access commitments should be included in Grant Agreement
▪ Foundation / Grantee agreements in place that provide for Global Access	• Grant Agreement • Global Access Strategy • Data Access Plan • Global Access License • Publication/Open Access • MOU	
▪ Grantee / Third Party agreements in place that provide for Global Access	• Clinical supply agreements • Clinical trial agreements • Technology Transfer agreements • Development Agreements • Regulatory Filings	

HUMAN FACTORS STUDY PLAN COMPLETED

GLOBAL DRUG DEVELOPMENT

Goal / Definition

Development of a plan for the conduction of Human Factors studies (Formative and Summative) throughout the program

A study conducted with representative users to assess the adequacy of the combination product user interface design to eliminate or mitigate potential use-related hazards.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
• Human Factors Study Plan completed	a) Intended use statement with benefit of medical device reflected, including consideration on training, education, experience, physical condition, and frequency of use b) User Requirements Specification (URS)	▪ Summary report containing key data / information or information to substantiate conclusions ▪ Illustrative data tables or figures may be reported in an appendix

IND-ENBALING STUDIES COMPLETED

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Non clinical safety data and rationale for dose selection.

Preclinical drug candidate development activities to support clinical evaluation completed.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Initial nonclinical pharmacological studies completed	a) General pharmacology and mechanism(s) of action b) Dose formulation and regimen c) PK, PD, ADME (e.g., biomarker ID, *in vitro* vs. *in vivo* assessments, animal model selection, modeling strategies, etc.) d) Off-target screening e) Bioavailability (i.e., tissue, serum, spinal fluid, blood-brain distribution, etc.) f) Development and qualification of supporting bioanalytical and analytical methods (e.g., IR, HPLC, GC, GC/LC MS, etc.) for animal and human application	▪ Pre-IND briefing package, if available; or ▪ Summary of key data to substantiate conclusions ▪ Illustrative data tables or figures may be reported in an appendix
▪ Initial nonclinical efficacy studies completed	a) Desired outcome measurement criteria b) Demonstration of statistically significant response c) Dose-response relationships & formulation dependency d) Equal or superior efficacy data in comparative studies against licensed and alternative treatments e) Development and qualification of supporting bioanalytical and analytical methods for animal and human application (may overlap with pharmacological characterization)	▪ As above
▪ Initial nonclinical safety / toxicity studies completed	a) Acute and sub chronic animal toxicology studies, *in vitro* and *in vivo* assessments (e.g., genotoxicity screens, dose-response relationships, etc.) b) Establishment of NOAEL, ideally assessing equal or superior safety / toxicity data in comparative studies against licensed and alternative treatments c) Development and qualification of supporting bioanalytical and analytical methods for animal and human application (may overlap with pharmacological characterization)	▪ As above

INITIAL DS/DP CHARACTERIZATION COMPLETE

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

To evaluate the drug substance (DS) and drug product (DP) that is well-characterized (stable with known impurity profile) and practical to administer in the clinic to ensure ready supply of drug of sufficient quality in Phase 1 clinical trials.

Clinical study start-up plan initiated with consideration of feasibility and identification of risks.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
• Initial drug product characterization completed	a) Delivery & formulation strategy to support animal and human studies (e.g., IV, injection, tablet, capsule, oral strip, inhalant, prodrug etc.; assess IP space if special delivery system) b) (For injectables) Consideration for hemolysis studies, adhesion of drug to delivery syringes, tubing, equipment, assess precipitation of drug at injection site (in vitro testing) c) (For prodrug) Characterization in vitro and in vivo conversion to active form d) Particle size considerations and formulation dependency (e.g. milling, micronization, etc.) e) Excipient selection and characterization f) Form-specific physicochemical properties (e.g., bulk & tap densities, flowability, compressibility, pXRD, IR, dissolution, disintegration, etc.) g) Form- and formulation-specific in-use stability studies h) Assess formulation bioavailability / PK for clinical dosing regimen, determine whether "blinding" of clinical formulation needed	▪ Summary of key data to substantiate conclusions ▪ Illustrative data tables or figures may be reported in an appendix
• Initial cGMP manufacturing process defined	a) Drug substance manufacturing process overview (e.g., synthetic pathways, intermediate selection, high-level description of unit operations and equipment) b) Drug product manufacturing process overview c) Documentation of external manufacturing plan via Partner Selection Milestone d) Reference standards, analytical GMP methods for drug substance and drug product release and stability, impurities specs for drug substance and drug product	▪ Initial cGMP manufacturing process defined
• GMP manufacturing	a) GMP DS and Ph1 DP released	▪ Summary of key data e.g. Certificate of Analysis

*Candidate progression is discussed at standing grantee update meetings with the investment team

PARTNER SELECTION PLAN IN PLACE

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Determine need for product development partner and plan for partner selection.

Partnership requirements plan completed.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Partnership requirements identified (high level)	a) Analysis to decide whether there is need to partner for product development to complement internal capabilities across all stages of drug development, which could include: • Functional activity partners such as CROs, CMOs, commercial biopharmaceutical companies, PDPs & out-licensers needed for discovery, preclinical & clinical development, manufacturing, delivery / uptake, etc. • Supporting activity partners such as IP, Legal, Regulatory, Global Access, etc. Firms / Agencies b) Partner capability requirements c) Potential partner shortlist	▪ List of internal capabilities and identified gaps
▪ Path & timing for partnership engagement identified (high level)	a) Partnership engagement path (e.g., BMGF network, academia, service providers) b) Timing and length of partnership engagements	▪ Up to one page description of partner engagement plan
▪ Anticipated partnership challenges and risks identified (high level)	a) Anticipated challenges, risks, and contingencies for product development b) Mitigation plan and trigger mechanisms	▪ Table summarizing risk, probability of occurrence, potential impact and mitigations

*Candidate progression is discussed at standing grantee update meetings with the investment team

PRE-IND MEETING SCHEDULED* (OPTIONAL)

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Gain concurrence with Regulatory Authority on Phase 1 study design.

Data Package necessary for pre-IND and/or IND meeting (or NRA equivalent meeting) submission, and/or meeting opinion.
(*Specific communication requirements of National Regulatory Authorities (NRAs) should be identified upon initiation of the Regulatory Strategy Plan)

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Package for pre-IND meeting submission (NRA equivalent meeting) prepared ▪ Ethics committee review process understood and interplay with pre-IND meeting understood	a) List of specific questions and input sought from regulatory agency b) Summary of drug characterization data (e.g., basic molecular properties, physicochemical properties, purity, stability, preliminary formulation concept, etc.) c) Summary of initial nonclinical assessments • PK, PD, ADME • Efficacy and activity • Safety d) Manufacture plan & initial specs developed as required for clinical trial supplies e) Outline of follow-on nonclinical studies f) Outline of clinical plan (which may leverage Clinical Development Plan and Clinical Readiness milestones content), including: • Rationale for intended use • Studies supporting dosing and duration • Appropriateness of safety monitoring techniques • Assurance of clinical trial supply quality • Phase 1 trial design & protocol • Inclusion / exclusion criteria; safety monitoring procedures • High-level plans for Phase 2 study	▪ Pre-IND briefing package
▪ Post-meeting debrief and development strategy adjustment (if required) completed	a) Review of decisions and recommendations made at the meeting b) Action plan to address highlighted development issues (if any) prior to filing of clinical trials application	▪ Regulatory responses to questions

REGULATORY STRATEGY AND PLAN IN PLACE

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Regulatory path and plan in place.

Plan for proposed regulatory path through life-cycle of the product.
(*An iterative document that is initiated at FIH, updated continually along the development process, and reviewed through to DTF)

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE

▪ Proposed regulatory path through life-cycle of product defined, including:
  ▪ Clinical development
  ▪ Licensure
  ▪ WHO PQ (if needed)
  ▪ Post-authorization safety surveillance and further product development
▪ Include any specific plans to use alternative development pathways (conditional, accelerated, breakthrough) or registration processes (article 58, tropical voucher, orphan)
	a) Prioritized list of countries where the drug is intended to be introduced[1]
	b) Understanding of country-specific regulatory requirements
	  • Type of submissions (original, supplement/variation, line extension, etc)
	  • **Significant / unique requirements[2]**
	  • Required HA communications and timing
	c) Plans for NRA engagement during development to gain feedback and agreement with development and filing strategy
	d) Key regulatory risks and risk mitigation plans
	e) Plan to ensure proposed indication and labeling aligns with TPP and donor/utilization requirements
	f) Plan for approval and protocol review for clinical trial starts in target countries
	g) Plan to handle monitoring and reporting of adverse events and safety issues during clinical trials and post-authorizations
	h) WHO PQ applicability/programmatic suitability, plan to pursue WHO PQ (if applicable)
	i) Plans for WHO PQ engagement by end of phase 2 (if applicable)
		▪ Updated throughout life-cycle of product reflecting new data and priorities as they develop
		▪ Required at each gate: Detailed plan with timeline and resources for the next phase of development (e.g. detailed plan for Phase 1 required at the FIH gate review), and high-level / draft plan focusing on risk identification and mitigation for all subsequent phases of development

Items in **bold** font reflect suggested reporting guidelines for this stage gate

[1]If India and China are among the likely target countries, content is required at FIH. Otherwise it applies at EP2.

[2]Specific requirements associated with Chinese Pharmacopeia should be updated early

STRATEGIC DEMAND FORECAST

GLOBAL DRUG DEVELOPMENT

Goals/Definitions

Business case for developing a deliverable product

Business Case, deliverability assessment, strategic demand forecast and COGS reports and cost effectiveness report

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Strategic Demand Forecast	• Methodology to be used to assess potential demand adjusted for product availability, country introduction decisions, uptake timing (without any supply or financing constraints) • BMGF provides a methodology grantees may use for demand forecasting • Demand forecast methods should align with to the BMGF valuation model (in Integrated Portfolio Management tool)	▪ BMGF provides methodology

STUDY START-UP ACTIVITIES INITIATED

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Start-up activities are initiated to enable timely. Phase 1 start.

Clinical study start-up plan initiated with consideration of feasibility and identification of risks.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Clinical trial designed	a) Protocol design and scope for Phase 1 (including study plans, medical monitoring plans, timelines and budgets) to support both NRA approval and WHO PQ b) An overview of the clinical development path (i.e., request for conditional approval) and rationales c) Updates to Investigator's Brochure for the next phase of development. (e.g., prior to First in Human include Core Safety Information from toxicology study)	▪ Protocol synopsis ▪ Investigator Brochure
▪ Clinical trial site feasibility completed	a) Plan for site assessment (may include audit) including considerations such as infrastructure, capability, supply chain feasibility, capacity, etc. b) Understanding of required approval process to conduct clinical studies at all potential study sites and identifying risks	▪ Summary report
▪ Clinical vendors/ CRO identified and site initiation activities conducted	a) Scope of work required (e.g., site selection, site initiation, data management, process & method development, etc.) and agreed metrics to monitor trial progress b) Partner engagement strategy (e.g., outsourced activity, insourced activity, consultation, etc.) c) Examples of past vaccine trial experience in the disease area/geographic area d) Understanding of the stepwise clinical trial approval process, engaging with local regulatory authorities, ethics committee etc. e) Existing network of investigators and study sites f) Audit record of clinical study sites and track record of staff GCP training g) Completion of site initiation activities	▪ Summary report
▪ Clinical assay readiness	a) Relevant clinical assays need to be available prior to entering clinical studies	▪ Summary of assay qualification

COMPLAINT HANDLING PROCESS DEFINED

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Ensure that product complaints are recorded, processed, and feed into a continuous improvement process for the product.

A system to address complaints related to the product. Components of the system include: process/procedure, trained personnel, and proper record keeping.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Complaint handling process defined	a) Establishment of appropriate infrastructure (e.g., acall center, return/ replacement process etc.) to handle consumerproduct complaints b) Definition of procedures to ensure that complaints are processed in auniform and timely manner c) Root cause analyses forproblems reported and feed back into a continuous improvement process to prevent future occurrences	

DELIVERY MILESTONES (TO BE IN "INTRODUCTORY PHASE")

GLOBAL DRUG DEVELOPMENT

GNG (Global Normative Guidance)	**Date when critical normative guidance (country adoption into national guidelines if in a single focal country, WHO policy guidance, SAGE recommendation, other) is announced publicly**
LFC (Launch in First Country)	Date when country or large-scale private agency formally incorporate product into system planning/financing (i.e., not temporary pilot, demonstration or operational research).
50% C (50% Coverage Achieved)	Date when anticipate achieving 50% of the program strategy team's coverage goal for the overall product class (see below) – i.e., fi the goal for rotavirus vaccines is 80% coverage in Gavi countries, then year X is when coverage is expected to achieve the half-way point (40% coverall in all, or 80% in half of Gavi countries); if the target is 20m male circumcisions in target geographies, then year Y when coverage is expected to achieve the half-way point (10m). Product class is defined as the general category that is the next order up from the candidate or product name. This is likely to align with how coverage tracked for a health intervention. Examples are rotavirus vaccine, HIV first-line drug, TB molecular diagnostic, etc. Please specify the product class in the "Target Coverage/Market Share Description" field.
TMS (Target Market Share Achieved)	Date when anticipate this specific product will achieve the target market share for the overall product class – i.e., Year X when Gene X-pert will represent 25% market share of all TB molecular diagnostics. This should be informed by a demand forecast and initially should mirror the assumptions made for impact modeling and should be refined over time with more concrete demand forecasts. Please leave blank if the team is agnostic as to coverage of the specific product and is more interested in overall coverage of the product class or if this is the only product class or if the team has not yet thought through these questions.

FULL-SCALE POST-LAUNCH MANUFACTURING STRATEGY UPDATED

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

An updated strategy to address operational readiness for full-scale manufacturing launch, as more information around identification commercial partners, launch markets and manufacturing scale based on strategic demand forecasts becomes available

Operational readiness for full-scale manufacturing
(*Full-Scale Post-Launch Manufacturing Strategy is initiated prior to the DTF gate review and is updated & reviewed again at PQ/LR gate review)

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
Commercial launch strategy	a) Product expiry date proposal/strategy for regulatory submission b) Commercial launch strategy for each country market c) Finished product Warehouse qualified and operational d) Shipping validation complete	▪ Summary report
Quality Assurance/Compliance activities	a) Product registration b) Facility audit reports c) Audit observation compliance (CAPA, if required) d) Pre-approval inspection strategy, clear roles and responsibilities of partner and CRO/CMO	▪ Summary report
Plan for ongoing CMC Support to ensure uninterrupted supply of high quality DP in all markets	a) Regular meetings with CMOs to monitor supply chain, review of quality incidents b) Ensure corrective actions such as improvements in systems/procedures, staff training c) Ensure timely support of technical support for manufacturing problems d) Evaluate process deviations/excursions during manufacturing that might affect quality e) Scientific evaluation of commercial product stability reports/problems f) Monitor and address changes in raw materials that affect manufacturing/product quality g) Timely submissions of periodic regulatory reports and regulatory agency interactions h) Assess impact of changes in Strategic Demand Forecast, determine whether alternate/additional manufacturing site or additional raw materials suppliers needed	▪ High level plan

Prior to PQ/LR stage gate, in collaboration with Regulatory, Compliance and other project team members, commercialization partner CMC will prepare a strategy for interactions with regulatory authorities related to regulatory review of registration documents and commercial manufacturing sites. CMC will update, as required, post-launch CMC support strategy

*Candidate progression is discussed at standing grantee update meetings with the investment team

PHARMACOVIGILANCE PLAN IN PLACE

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Develop a plan for pharmacovigilance activities.

Systems and processes that ensure that information about all suspected adverse reactions that are reported, collected and collated in an accessible manner.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Pharmacovigilance plan in place	a) Process to collate and review complaints to determine if they represent reportable adverse drug events b) Process to report adverse events to the appropriate regulatory authority bodies (e.g., for FDA - CDER, CBER, CDRH) c) Develop a strategy to maintain compliance with annual reporting requirements (e.g., Product Safety Update Reports filing for the drug component)	

WHO PQ OR FIRST LOCAL REGISTRATION

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

WHO PQ dossier submission.

WHO PQ meeting data submission, and/or meeting decision and recommendations for product prequalification.
(Note: PQ meeting with QSS conducted at the end phase 2)

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Safety and efficacy demonstrated	a) Safety and efficacy data from all clinical trials b) Product release specifications (including pre-approval inspection of manufacturing facilities) c) Stability data to support expiration dating (e.g., cold chain requirements/suitability for use under field conditions, shelf life and remaining shelf life at time of shipment)	▪ Notification of submission date
▪ Relevance to target population demonstrated	a) Relevance of the available clinical data to the UN target population b) Specific requirements of UN procurers c) Any specific advisory group recommendations needed/documented/addressed	▪ Summary of special requirements met
▪ WHO tender specifications met	a) Packaging: Volume of cold space required (if any), primary and secondary packaging characteristics b) Suitability of presentation (e.g., tablets, vials, ampoules or prefilled auto-dispensable syringes) c) Applicability packaging requirements d) Adequacy of information on labels for package: all relevant information is stated, insert reflects product characteristics and does not contradict model inserts and WHO policies; availability in all required languages e) Tertiary packaging prepared according to the WHO shipping guidelines and are properly validated	▪ Summary of product suitability requirements met
▪ Pharmacovigilance (PV) Plan	Particularly relevant if the drug is intended for launch only in low income countries where passive PV is insufficient. Plan can include: a) Summary of key identified and potential risks b) Action Plan for collecting reports of adverse reaction, active monitoring, evaluating and reporting of safety issues to regulatory authorities (e.g., Periodic Safety Update Reports, ADRs: Adverse Drug Reactions) c) Overall PV plan for the product bringing together the actions for all individual safety issues	▪ High level plan