MOR106-CL-102
Unblinded Site Staff Training

Moving Potential. Forward.

Protocol Code: MOR106-CL-102

- **Protocol Title: A parallel-design phase 1 study to assess safety, tolerability and pharmacokinetics / exposure following different dose levels of MOR106 (administered subcutaneously or intravenously) in healthy male subjects (open label, single dose), and in subjects with moderate to severe atopic dermatitis (randomised, placebo-controlled, double-blind, repeated dosing)**

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Novella Unblinded Study Team Contacts

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Protocol Overview

MOR106-CL-102

Study Objectives

- Primary objective
  - Part 1 - Healthy Male Subjects
    - To evaluate the safety and tolerability of single doses of MOR106 administered s.c. in comparison to i.v. in healthy male subjects and to evaluate the PK of single doses of MOR106 s.c., including the determination of the relative bioavailability of MOR106 after s.c. administration .
  - Part 2 - AD Subjects
    - To evaluate the safety and tolerability after multiple s.c. doses of MOR106 given to subjects with moderate to severe AD, compared to placebo.

MOR106-CL-102

Study Design Overview

- Part 2 (AD subjects)
  - 45 subjects (2:1 randomization)
  - 12 week treatment period
  - 16 week follow up period
  - MOR106 320 mg (2 mL at 160 mg/mL) Q2W SC injection (+ loading dose at first administration) vs placebo

MOR106-CL-102

Analysis

Interim analysis in AD subject treatment group:

- to feed the End of Ph2 meeting
- Interim analysis performed after 8 weeks of treatment (D57)
- In addition to the primary analysis (at the end of the 12 weeks treatment period) and the full analysis (including the 16 weeks follow-up period).

MOR106-CL-102

Additional exploratory arm (optional)

- To allow testing of an additional SC dose in the event the current 201 study results indicate that we have a gap in the dose range we need to evaluate
- To assess the lower range of drug exposure
- IV or SC administration of MOR106 - frequency of administration to be defined (based on results of ongoing 201 study)
- 45 additional AD subjects (2:1 randomisation)

Schedule of Assessment

- 4-week screening period
- 12-week treatment period
- 16-week follow-up
- Subjects to remain on site until 2 hours after dosing is completed D1
- Subjects to remain on site until at least 1 hours after dosing is completed all subsequent dosing visits

EVENT	SCR	TREATMENT PERIOD[1]							FOLLOW-UP PERIOD							
Visit Day[2]	-28 to -7	1	15	29	43	57	71	85/ET D[3]	99	113	127	141	155	169	183	197[4]/ED[5]
Study Visit	Screening	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15[4]/ED[5]
Informed consent	X															
Inclusion/exclusion criteria	X	X														
Demographics	X															
Medical history	X															
Physical examination	X	X	X[6]	X	X[6]	X	X[6]	X	X[6]	X[6]	X[6]	X[6]	X[6]	X[6]	X[6]	X
Vital signs[7]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Height and weight[8]	X			X		X		X								
12-lead electrocardiogram	X	X[9]			X[9]			X				X				X
Serology[10]	X															
Pregnancy testing[11]	X	X		X		X		X		X						X
Clinical laboratory safety tests	X	X[12]	X[12]	X[12]	X[12]	X[12]	X[12]	X	X		X		X		X	X
Clinician-reported outcomes (EASI, IGA, SCORAD, BSA)	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Subject-reported outcomes (POEM / DLQI / short ACQ[13] / SNOT-20[13])		X	X	X	X	X	X	X	X		X		X		X	X
Train and check compliance of ePRO diary use[14]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Pruritus NRS[15]																
Provide Subject Participation Card	X															

1 The end of the treatment period (Day 85 visit) is considered to be reached 2 weeks after the last dose which is on Day 71 visit.
2 A window of ± 2 days is allowed for all visits up from Visit Day 15 (included). Visit dates are always calculated from Day 1 (unless subject discontinues early and attends ETD). If a subject has an ETD visit, the follow-up visits are performed 14, 28, 42, 56, 70, 84, 98 and 112 days after the ETD visit.
3 Subject who are discontinued from treatment during the dosing period will perform Day 85/ETD visit (14 days after the last dose) as the last visit in the dosing period before entering the follow-up period.
4 End of Study visit.
5 Early discontinuation visit, if applicable.
6 During these study visits, a targeted physical examination, consisting of cardiovascular, respiratory and gastrointestinal examination will be performed.
7 Vital signs are defined as supine heart rate, blood pressure (systolic and diastolic) and tympanic temperature.
8 Height only at screening
9 At Day 1, ECG to be taken before dosing and approximately 1 hour after dosing. At Day 43 visit before dosing.
10 Serology sample for hepatitis B surface antigen, hepatitis B core antibody, and hepatitis C virus antibody, and human immunodeficiency virus 1 and 2 antibodies and Quantiferon testing
11 Females of childbearing potential only. Serum pregnancy test at screening, urine test before dosing on Day 1 and at all time points thereafter.
12 On dosing days, hematology, biochemistry, and urinalysis are to be done prior to dosing.
13 Only applicable for subjects identified with asthma or rhinosinusitis at screening.
14 Training will occur at screening, and will be repeated at any visit when deemed necessary.
15 Pruritus NRS should be assessed twice daily (morning and evening) from screening to Day 197/ED visit.

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Investigational Product

Study Design MOR106-CL-102 part 2

- Multiple-dose blinded study in AD patients
- Multiple sites (±14) in UKR, DE, SP, and UK
- 45 subjects / 2 groups: MOR106 : PBO = 2:1

	Treatment period						
Study Day	**1**	**15**	**29**	**43**	**57**	**71**	**85/E TD**
Study Visit	**1**	**2**	**3**	**4**	**5**	**6**	**7**
Group 1	640 mg MOR106 (LD)	320 mg MOR106	320 mg MOR106	320 mg MOR106	320 mg MOR106	320 mg MOR106	-
Group 2	Placebo	Placebo	Placebo	Placebo	Placebo	Placebo	-

General Information

- Two IMPs used: active (MOR106) and Placebo
- Fixed dose
- Six doses given every 2 weeks
- Loading dose at visit 1
- IMP is prepared by unblinded nurse or pharmacy staff
- IMP administration is performed by unblinded nurse
- IMP administered via Sub Cutaneous injection
- Instructions provided in Pharmacy Manual

Site Blinding Plan

- **A template Site Blinding Plan will be provided to each site for developing the site specific Site Blinding Plan**
- **Collects the necessary detail of the plan to ensure accidental or unintentional unblinding is avoided**
- **Created by blinded and unblinded study team – training to be provided to both blinded and unblinded study team**
- **Copy filed in Pharmacy Binder (unblinded) and Reference Binder (blinded)**
- **Will be checked during the study by CRA and UCRA for compliance and for updates needed**

Hazards of MOR106 Drug Product

- **MOR106 is an experimental therapeutic humanized IgG1 antibody directed against IL-17C**
- **MOR106 is not an hazardous drug as shown in MSDS (Annex 1 of the Pharmacy Manual for MOR106 SC Solution)**
- **Caution should be taken to minimise accidental exposure**
- **Intakes, inhalation, and contact with skin and eyes must be avoided**
- **It is recommended that a laboratory coat, safety glasses (or alternatively behind glass of the laminar flow cabinet) and powder-free gloves should be worn when handling the preparations**

Description of MOR106 and placebo

- **MOR106 is a solution for SC injection**
- **Single-use vial of 160 mg/mL MOR106 in a buffer with an extractable volume of >= 1.0 mL**
- **Storage condition: 2-8 ^{0}C**
- **Placebo = Formulation buffer without active pharmaceutical ingrediant**
- **Identical storage conditions are used as active and placebo**

Description of MOR106 and Placebo

- **DIN 2R Type I uncoloured glass vial**
  - **Rubber stopper**
  - **Aluminum crimping cap**
  - **Light blue flip-off seal**
- **Nominal volume: 1.0 mL**

MOR106 without label

- **Placebo:**
  - **filled in identical container, stopper, cap and seal as active**
  - **identical nominal volume as active**

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Description of MOR106 and Placebo

- **Visual distinction can be made between vials with active and placebo**
- **Study medication will be supplied to the site pharmacy as "open label" medication**

	MOR106 160 mg/mL	Placebo
Appearance	Colorless to light yellow/brownish	Colorless
Viscocity	High	Low
Identification	Batch number on Alu cap	None
Injection Force	High	Low

Description of MOR106 and Placebo

- **MOR106 SC vials**
  - **Manufactured by Rentschler (Germany)**
  - **2 vials / carton box**
  - **Packaging & labeling CSM Germany**
  - **EU QP release by CSM Belgium**
  - **CSM depot in Germany, Avinex depot in Ukraine**
  - **Elpro temperature monitor device**

IMP Shipment

- **Triggered by regulatory green light and site activation in IWRS by GLPG/Novella**

- **Shipment of IMP and medical materials to the clinical site:**
  - **SC medical kits shipped (for administration of 100 doses) including safety stock depending on expected enrollment rate**
    - 3 mL syringes with Luer lock
    - needle 21 G x 1” with needle shield
    - Needle 26 G x ½” for SC injection

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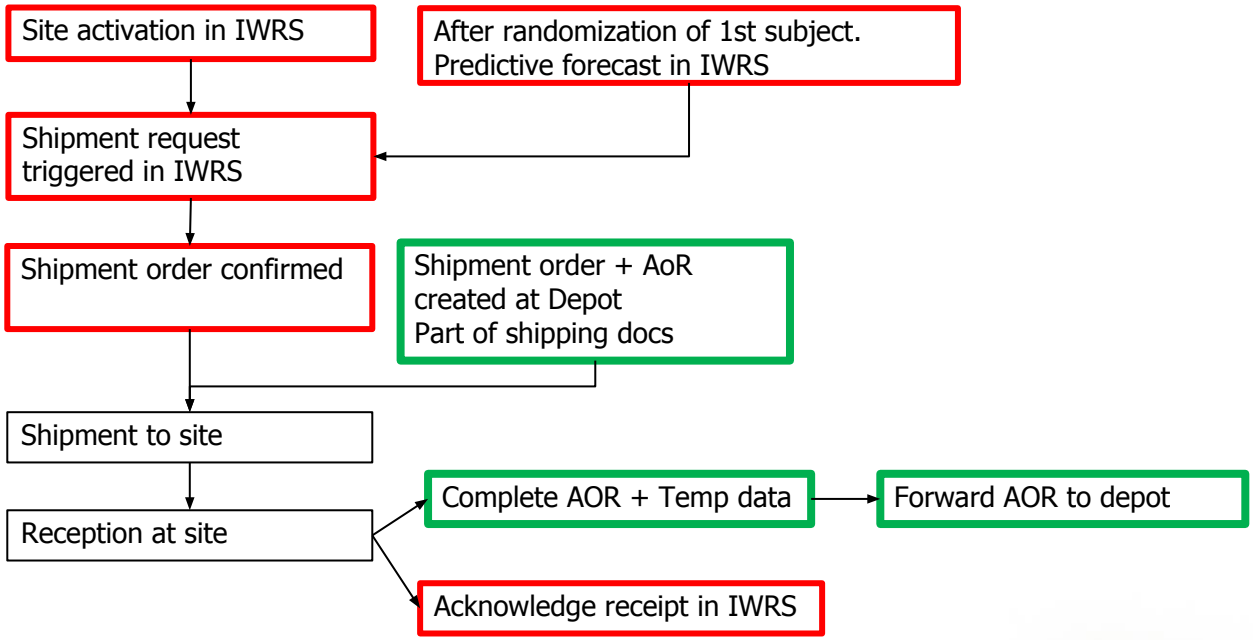
IMP distribution + receipt



Ancillary supplies

Site activation in IWRS

Shipment request triggered in IWRS

Shipment order confirmed

For IMP see previous slide

1st shipment to site in ERP system triggers shipment order for ancillary supplies
AoR created at Depot
Part of shipping docs

Shipment to site

Reception at site

Complete AOR

Forward AOR to depot

IMP supply management

- **Clinical supply will be managed in IWRS (Endpoint Clinical) – initial supply and automatic re-order**
- **Receipt of IMP, storage, handling, accountability, preparation, administration and return will be done by the unblinded site team**
- **Verification of the IMP storage conditions, accountability and final reconciliation will be done by the unblinded CRA**
- **After final reconciliation by unblinded CRA and approval of destruction by GLPG, the unblinded CRA will arrange shipment of all used and unused IMP back to CSM for destruction**

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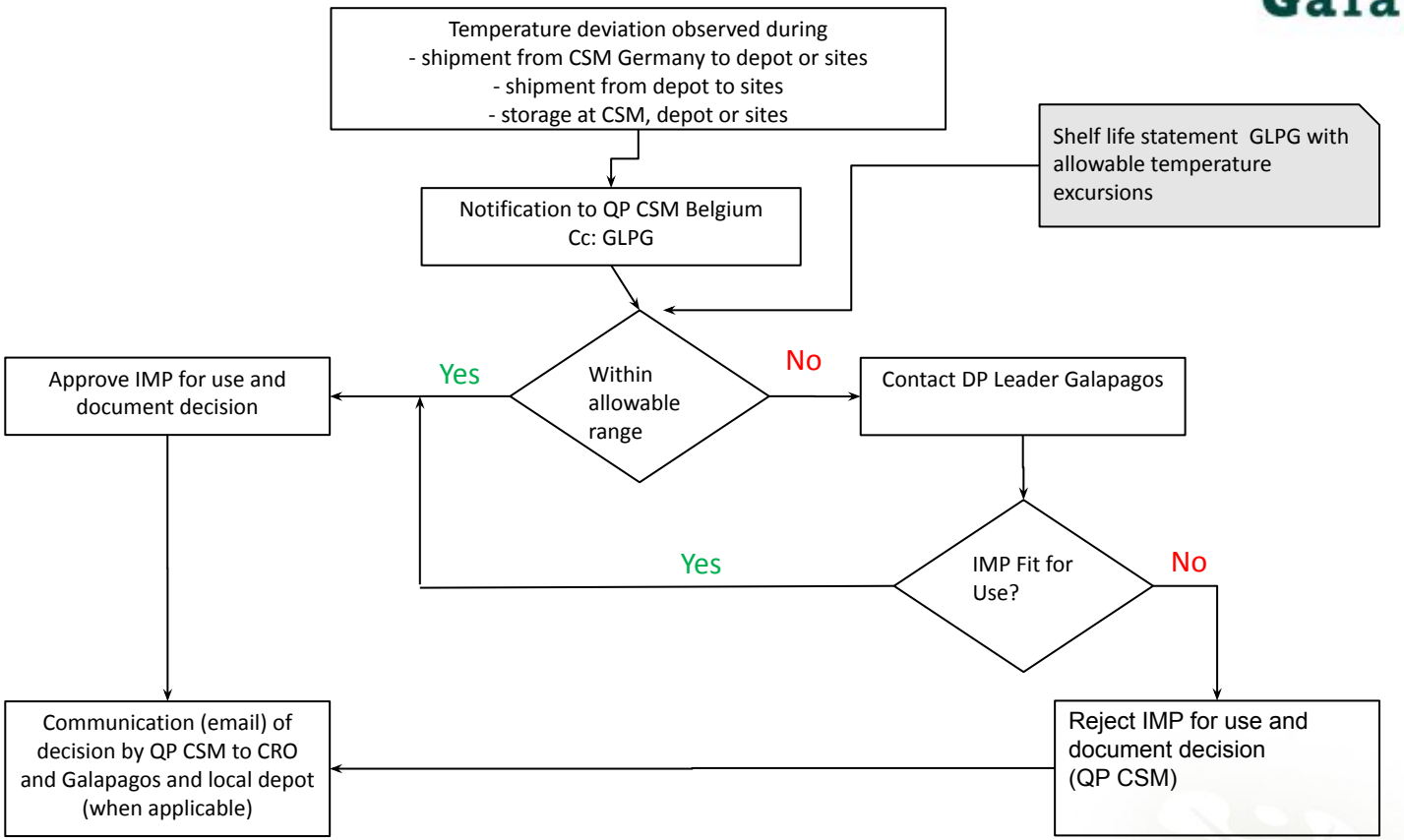
IMP receipt, storage and re-order

- An accountability form will be maintained to document the receipt, dispensing and return to Pharmacy of used/unused vials
- Temperature monitoring of the IMP will be performed (monthly downloads to be printed and signed and filed in Pharmacy Binder)
- Temperature excursion notifications are managed via IWRS
- Quarantine log provided to document the date and time of transfer from main stock to quarantine (labels to be used are in Pharmacy Manual) and back to main stock

Temperature Deviation Handling



Dosing Summary

- **Subjects will be dosed with two times 2 mL of active (640 mg) or placebo at visit 1 using SC injection (Loading dose)**
- **At subsequent visits 2-6, subjects will be dosed with one time 2 mL of active (320 mg) or placebo**
- **Syringes and needles are provided by the sponsor:**
  - **3 mL syringes with Luerlock for secure connection with needle**
  - **Wide bore needle (21 G x 1”; with needle shield) for collection of active or placebo from vial**
  - **Suitable needle (26 G x ½”) for SC injection**

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IMP Preparation Key Steps

- Unblinded study team members will receive an automatic notification from IWRS with the treatment allocation, kit numbers to be used etc

- The Preparation and Administration form will be used to document the process

- IMP kits are removed from refrigerator (record time) and allowed to adjust to room temperature for 30-60 mins. They should not be visible to the blinded team (consider location, box, ..)

- Syringes for administration prepared (record time, date and person preparing), kept at room temperature and placed in a suitable light protecting box for transportation to the subject

IMP Preparation Key Steps

- **IMP should be administered within 2 hrs after start of preparation (time removed from refrigerator)**
- **Date, time, name of unblinded nurse and injection site also recorded in subject source notes (will be entered in the eCRF)**
- **All used vials will be packed in plastic bags and labeled with subject label and will be stored (ambient – uncontrolled) for reconciliation by the unblinded CRA. They should not be visible to the blinded team (consider location, box, ..)**

IMP administration via SC injection

- SC injection in the upper or lower abdominal area only
- Different quartiles are used to inject and are rotated each time – documented in notes by unblinded IP administrator
- A standard 45% angle and lifted skin fold are used for SC injection
- Internal procedure should be used for SC injection

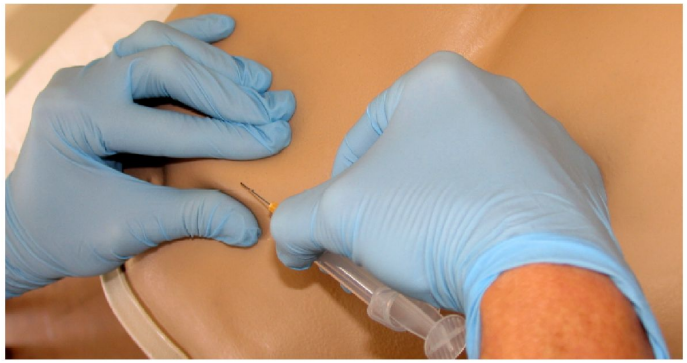
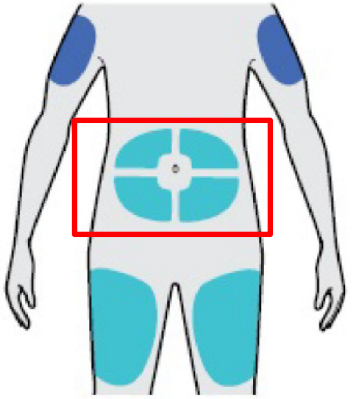


Figure 1: Gently pinch the skin up into a fold. Insert the needle into the skin at an angle of 45º (unless giving insulin which should be at 90º as a shorter needle is being used)



= Self-injection or by caregiver

= Injection by caregiver only

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IWRS Endpoint

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IRT Basics

IRT (Interactive Response Technology) is an integrated web system designed to manage subject transactions (screening/rescreening/randomization/subject visit/completion), drug dispensation and inventory supply.

IRT Access:
https://secure.endpointclinical.com

After documented training

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System Overview

Site Access	Functionality
Subject Management Blinded staff: Study Coordinator/Investigator	Screening Screen Failure Rescreening Randomization Visit Day 1 Treatment Discontinuation Subject Visit Completion Unblinding
Inventory Management Unblinded staff: Pharmacy	Drug Receipt Manage Inventory Subject Kit Replacement
Notifications	Sent After Each Transaction
Web Reports	Blinded web reports Unblinded web reports

Key Identifiers

Identifier Type	Length	Range
Site ID	6	Three letter ISO country code +3 digit sequential number. GBR001
Subject Number	9	Assigned by IRT at Screening. GBR001001 - GBR001999 GBR002001 - GBR002999
Randomization Number	5	10001-99999
Shipment Number	5	Found on Shipment Packing Slip Ex: 10001 - 19999
Kit Number	3	Assigned at Randomization, Subject Visits, and Subject Kit Replacement Ex: 001 - 800

IRT Access

High Level	Details
Sent Via Email	You Must have a Secure, Non Shared Email Account
Initial Temporary Password	Update Upon 1st Access by IRT URL Password: Minimum 8 Digits with Number and Symbol
Security	**Do Not Share your Access Information!**

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Randomization Notifications

- **Dispensation information is NOT displayed on IWRS screen**

- **Notifications:**
  - **Part 2 Blinded Notification**
  - **Part 2 Unblinded Notification**

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Example Randomization notification (UnBlinded)

Galapagos MOR106-CL-102

***** THIS IS AN UNBLINDED NOTIFICATION *****

Investigator Name:
Location:
Site Number:
Country:

Subject Number:
Year of Birth: YYYY
Subject's Age at time of Informed Consent:
Gender:
Planned Next Visit Date:

Screening Date: [System Date]
Randomization Date: [System Date]
Rand ID:

Part Description:

Treatment Group Assigned:

Kits Assigned:

Kit Description	Kit Number or Quantity of Lot Number	Lot Number	Expiry Date	Current Status
Kit UnBlinded Description	101	LOT03	31Dec2020	Assigned

Please see instructions for use in Pharmacy Manual.

Transaction Recorded Date/Time: [Site Local Time]
User Name: [First Name Last Name]
[Display 3]

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Example Subject Visit Notification (UnBlinded)

Galapagos MOR106-CL-201

***** THIS IS AN UNBLINDED NOTIFICATION *****

Investigator Name:
Location:
Site Number:
Country:

Subject Number:
Year of Birth: YYYY
Subject's Age at time of Informed Consent:
Gender:

Screening Date: [as entered by the user]
Randomization Date:

Visit Number:
Visit Name:
Visit Date: [as entered by the user]
Planned Next Visit Date: [Display n/a if this is the last visit for the subject]

Part Description:
Treatment Group Assigned:

Kits Assigned:

Kit Description	Kit Number or Quantity of Lot Number	Lot Number	Expiry Date	Current Status
Kit UnBlinded Description	100	LOT01	31 Dec 2020	Assigned

Please see instructions for use in Pharmacy Manual.

Transaction Recorded Date/Time: [Site Local Time]
User Name: [First Name Last Name]

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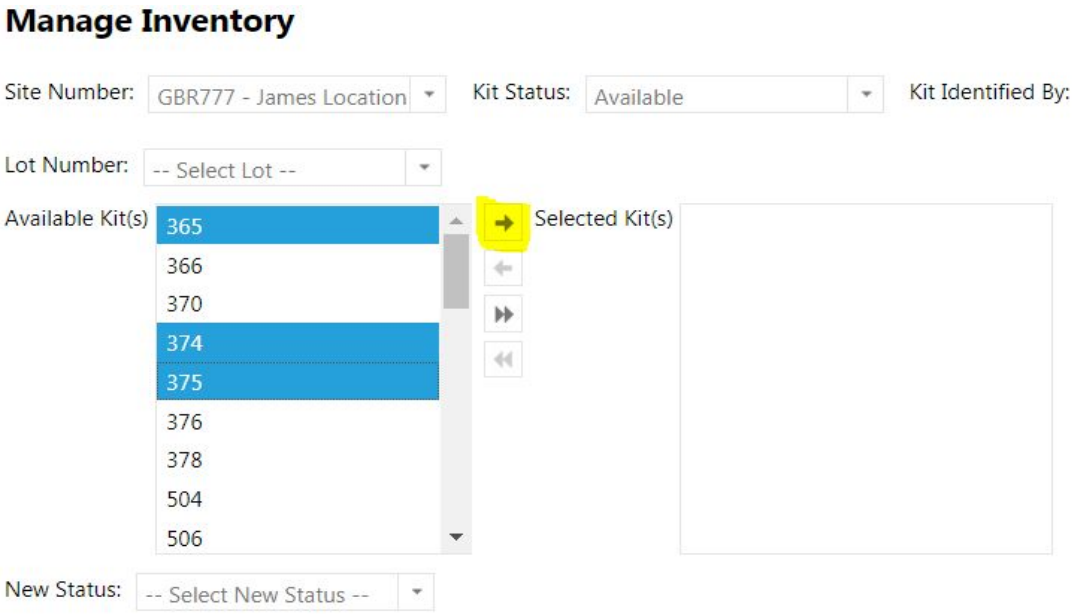
Drug Receipt

User Entry	Details
Drug Shipment Number	5 Digits
Complete and Intact	Yes or No
	If No: Enter affected Kit or Number of kits
Any Additional Lost/Damaged	Yes or No (repeat as necessary)
Temperature Alarm triggered	Yes or No. Selecting yes will put the whole shipment as quarantined until released by the Clinical Supplies Manager
IRT Marks Shipment as Received	

Note: shipments must be acknowledged in the IWR system prior to any randomizations

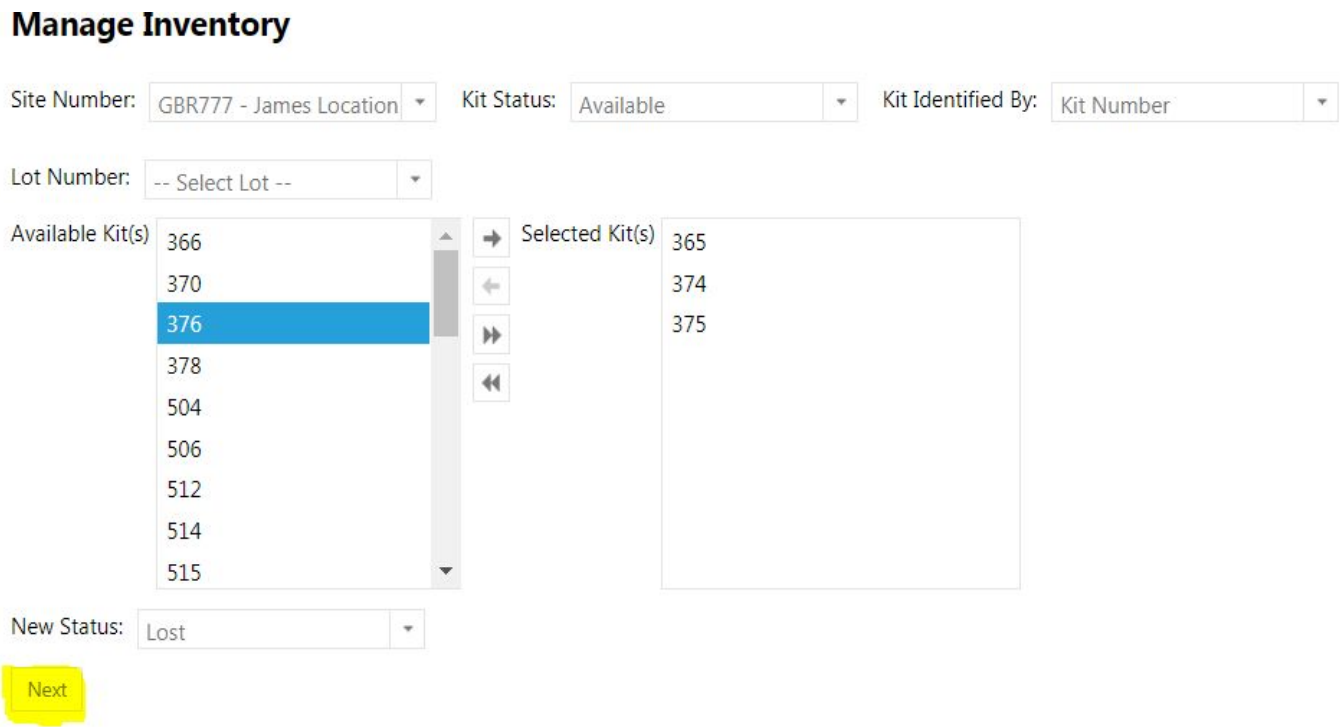
Manage Inventory

- Select Site Number, Kit Status, and Kit Type
  - Select Lot Number and Batch Number for further filtering
- Highlight desired kit numbers to update
- Ctrl or Shift buttons to select multiple kits
- Select single arrow to move selected kits to right-side box to be updated.
  - To move all kit numbers select the double arrow



Manage Inventory by Kit Number

- Select new kit status
- Select ‘Next’
- Review all data then select ‘Confirm’



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Subject Kit Replacement

User Entry	Details
Screening Number	Assigned by IRT at Screening
Confirm Subject Demographics	YOB, Gender
Select Kit Type	For Part 2 subjects, please select ‘Numbered Kit’
Select Damaged or Lost for kit	Kit number of damaged/lost kit selected.
Status of kit	Select Lost or Damaged for Kit or Device.
IRT Provides Replacement and Marks Lost/Damaged	
System triggers a blinded and unblinded notification following successful transaction	

Subject Replacement Visit Notification

- **Dispensation information is NOT displayed on IWR screen**

- **Notifications:**
  - **Blinded Notification**
  - **Unblinded Notification**

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Example Subject Kit Replacement (UnBlinded)

Galapagos MOR106-CL-102

***** THIS IS AN UNBLINDED NOTIFICATION *****

Investigator Name:
Location:
Site Number:
Country:

Subject Number:
Year of Birth: YYYY
Subject's Age at time of Informed Consent:
Gender:

Lost/Damaged Kits:

Kit Description	Kit Number or Quantity of Lot Number	Lot Number	Expiry Date	Current Status
Kit UnBlinded Description	123	LOT01	31 Dec 2020	Damaged

Replacement Kits:

Kit Description	Kit Number or Quantity of Lot Number	Lot Number	Expiry Date	Current Status
Kit UnBlinded Description	246	LOT01	31 Dec 2020	Assigned

Transaction Recorded Date/Time: [Site Local Time]
User Name: [First Name Last Name]

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Notifications and Web Reports

Notifications
Sent After Each IRT Transaction (ex: Screening)
IRT Access Info
IRT Access Info Reset
Drug Shipment Non Receipt
Drug Expiry Alert

Web Reports
Site Summary and Site Details Blinded Subject Summary and Subject Details Blinded Subject Visit Summary Blinded Site Supply Summary and Supply Details Blinded Shipment Summary and Shipment Details Blinded
Real Time Data
Export to Word or Excel
Additional Reports for Study Team

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Data Changes and Training Materials

Important Highlights – Data Change Forms
Data Change Form Accessible Via Support Tab on IRT Website
Fill Out Completely
Must Be Approved by Study Manager (blinded changes) or Unblinded Monitor (for unblinded data changes) for Processing

Important Highlights – Training Materials
Accessible Via Support Tab on IRT Website
Worksheets
Site User Manual

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Technical Support

Important Highlights
Endpoint provides 24-hour support by phone and email
Toll-free numbers are included on IRT Training Materials. For the most up to date, country specific, dial-in information please refer to the following link: http://www.endpointclinical.com/help-desk
Non Urgent Issues may be sent via email to: support@endpointclinical.com

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Monitoring Expectations

Blinded vs Unblinded

Both at Galapagos and Novella there will exist two **separate teams** for this study: **Blinded and Unblinded**.

- Blinded CRA:
  - Main point of contact
  - Frequent visits (approx. 1 visit every 4/6 weeks, but this depends on enrollment, issues at site)
  - No access to IP or Pharmacy Binder

- Unblinded CRA:
  - Max of 4 expected visits at the site
  - IP accountability and storage
  - IP preparation and administration
  - Final reconciliation and return

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Source Documentation and GCP

- **Document it!**
- **All original documentation must be retained – the first place the data is recorded = source**
- **Certified copy – a copy of the original record that has been verified (by dated signature or generation via a validated process) to have the same information as the original**

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Source Documentation and GCP

- **Source documents should be ALCOA-C**
  - **Attributable – who created the record and when, if the record was changed, who changed it, when and why**
  - **Legible – easily read**
  - **Contemporaneous – records made as they are observed, dates added**
  - **Original**
  - **Accurate – high level of integrity and honesty, thorough and correct**
  - **Complete**

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