Pharmacy Manual

Protocol Title: A Phase 3, Randomized, Multi-center, Open-label Study of DB-1303 Versus Investigator's Choice Chemotherapy in Human Epidermal Growth Factor Receptor 2 (HER2)-low, Hormone Receptor Positive (HR+) Metastatic Breast Cancer Patients whose Disease has Progressed on Endocrine Therapy (ET) (DYNASTY-Breast02)

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DUALITYBIO INC.

PHARMACY MANUAL REVISION HISTORY

Version Number	Version Date	Revision Comment
1.0	09-Sep-2023	Initial version
2.0	8-Feb-2024	Appendix 1, 2, 4 and 5 were updated Section 4.2 was updated IP storage and return was updated

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LIST OF ABBREVIATIONS

Abbreviation	Definition
ADC	Anti-drug Conjugate
DNA	Deoxyribonucleic acid
D5W	Dextrose 5% in Water
AE	Adverse Event
CPM	Clinical Project Manger
CRO	Contract Research Organization
CRA	Clinical Research Associate
CSTD	Closed System Transfer Device
CTA	Clinical Trial Agreement
CV	Curriculum Vitae
eCRF	Electronic Case Report Form
EC	Ethics Committee
GCP	Good Clinical Practice
GMP	Good Manufacture Practice
HER2	Human epidermal growth factor receptor 2
IB	Investigator's Brochure
IgG1	Immunoglobulin G1
IP	Investigational Medicinal Product
IRB	Institutional Review Board
IRT	Interactive Response Technology
ISF	Investigator Site File
IV	Intravenous
USP	United States Pharmacopoeia
PI	Principal Investigator
PK	Pharmacokinetic
PM	Project Manager
PVC	Polyvinyl chloride
RTSM	Randomization and Trial Supply Management
SAE	Serious Adverse Events

1. Introduction

This is a Phase 3, Randomized, Multi-center, Open-label Study of DB-1303 Versus Investigator's Choice Chemotherapy in Human Epidermal Growth Factor Receptor 2 (HER2)-low, Hormone Receptor Positive (HR+) Metastatic Breast Cancer Patients whose Disease has Progressed on Endocrine Therapy (ET) (DYNASTY-Breast02).

This document covers the description, labeling, shipping, storage, preparation, administration, and the overall accountability, return and destruction of the investigational product (IP), DB-1303 for Injection and Paclitaxel, Capecitabine and Nab-paclitaxel.

2. Subject Number Information

Each subject will be identified by a unique subject number consisting of a 10-digit number including the '-', of which the first 6 stand for the site number starting with the 2-digit country code. The last 3 of the subject number stands for the screening sequence from each site. For sites without satellite sites or the main site of satellite sites, the middle X is 0. For sites with satellite sites, the middle X is English number starting from a till z.

Example:
Site without satellite sites or main site of satellite sites: 8601-0-001
Site with satellite sites: 8601-a-001, 8601-b-001

The investigator or delegated site staff will assign the subject number individually and sequentially for all subjects. It is important to ensure there is no duplication in the allocation of a subject number.

3. Site Staff Training and Delegation

Prior to initiating any study-specific activities, site personnel will receive protocol-specific training which will be documented on a training log and system generated training courses before an access can be granted. And a delegation of authority log will be completed outlining the responsibilities and study procedures delegated by the PI to site staff.

4. IP Product Information

4.1. General Description

DB-1303, developed by DUALITYBIO INC. ("Duality", the Sponsor), is an antibody-drug conjugate (ADC) comprised of a humanized anti-HER2 (Human epidermal growth factor receptor 2), IgG1(Immunoglobulin G1) monoclonal antibody (trastuzumab biosimilar) covalently linked to a proprietary DNA topoisomerase I inhibitor (a derivative of exatecan) via a cleavable tetrapeptide linker.

DB-1303 will be supplied by Duality as a 100 mg lyophilized powder for infusion after reconstitution and dilution. The reconstituted drug product is a clear and colorless to yellow liquid and practically free from visible particles.

The investigator's choice chemotherapies, paclitaxel, capecitabine and nab-paclitaxel, will either be locally sourced or centrally supplied by Duality and will be administered according to local prescribing information

or treatment guidance in general use by the investigation site or drug label and pharmacy manual for centrally sourced medications.

4.2. Shipment and Receipt

IP will be supplied to study sites after all required study start up procedures are completed. Once the required start up procedures are completed, IQVIA Clinical leads or Project Leads when Clinical leads are not available will mark site as "Active" in RTSM and also would update the recipient contact details and an email is sent to the DUALITY supply manager (Juan Li: juan.li@dualitybiologics.com) to generate the initial IP shipment. Subsequent orders will be initiated by the site via Randomization and Trial Supply Management (RTSM) system or in some urgent cases via manual order, for which CRA/Site staff should send an email directly to DUALITY supply manager (Juan Li: juan.li@dualitybiologics.com) and the specific depot to indicate the quantity, drug type, site number, site recipient address and contact person, and expected arrival date with IQVIA clinical lead on the copy. If site inventory hits the minimal stock, it will trigger an order automatically to make up the inventory to the maximum stock

Article Type	Initial Stock	Minimum Stock	Maximum Stock	IRT Supply Name	Applicate country
DB-1303 option 1	20 vials	8 vials	40 vials	DB-1303 only-20	USA & Other sites that only require DB-1303
DB-1303 option 2	40 vials	8 vials	60 vials	DB-1303 only-40	USA & Other sites that only require DB-1303
Canada-DB-1303 option 1	20 vials	8 vials	40 vials	Supply Plan-CA-20	Canada
Canada-Paclitaxel	10 vials	4 vials	20 vials		
Canada- Capecitabine	1 carton	0 carton	4 cartons		
Canada-Nab-paclitaxel	10 vials	4 vials	20 vials		
Canada-DB-1303 option 2	40 vials	8 vials	60 vials	Supply Plan-CA-40	Canada
Canada-Paclitaxel	10 vials	4 vials	20 vials		
Canada- Capecitabine	1 carton	0 carton	4 cartons		
Canada-Nab-paclitaxel	10 vials	4 vials	20 vials		
China-DB-1303 option 1	20 vials	8 vials	40 vials	Supply Plan-China-20	China
China-Paclitaxel	20 vials	10 vials	30 vials		
China- Capecitabine	15 cartons	4 cartons	30 cartons		
China-Nab-paclitaxel	10 vials	4 vials	20 vials		
China-DB-1303 option 2	40 vials	8 vials	60 vials	Supply Plan-China-40	China
China-Paclitaxel	20 vials	10 vials	30 vials		
China- Capecitabine	15 cartons	4 cartons	30 cartons		
China-Nab-	10 vials	4 vials	20 vials		

paclitaxel					
EU/ROW -DB-1303 option 1	20 vials	8 vials	40 vials	Supply Plan-EU/ROW-20	EU/ROW
EU/ROW- Paclitaxel	20 vials	8 vials	30 vials		
EU/ROW- Capecitabine	2 cartons	0 carton	4 cartons		
EU/ROW-Nab-paclitaxel	10 vials	4 vials	20 vials		
EU/ROW -DB-1303 option 2	40 vials	8 vials	60 vials	Supply Plan-EU/ROW-40	EU/ROW
EU/ROW- Paclitaxel	20 vials	8 vials	30 vials		
EU/ROW- Capecitabine	2 cartons	0 carton	4 cartons		
EU/ROW-Nab-paclitaxel	10 vials	4 vials	20 vials		

Orders (initial and subsequent) will be sent to the email address as below.

Depot	**Countries**	**Email Address**
STZ	China (Mainland)	Shanghai02.DistributionRequests@catalent.com
SNG	Australia	Singapore.DistributionRequests@catalent.com
	Hong Kong	Singapore.DistributionRequests@catalent.com
	South Korea	Singapore.DistributionRequests@catalent.com
SCH	Belgium	Schorndorf.DistributionRequests@catalent.com
	France	
	Germany	
	Hungary	
	Italy	
	Poland	
	Spain	
KCM	Canada	KansasCity.DistributionRequests@Catalent.com
	USA	
BTH	UK	Bathgate.DistributionRequests@catalent.com
Catalent 3rd-party depot	Turkey	depot-tr@oximio.com
Catalent 3rd-party depot	Israel	depot-il@oximio.com

Size of each IP box:

China depot

Item Description	Length (cm)	Width (cm)	Height (cm)
DB-1303	4.7	4.7	7.5
CAPECITABINE 500MG BU 1X KT	13.5	2.8	7.5
PACLITAXEL 30MG/5ML	5.5	4	7.5
Nab-PACLITAXEL 100MG	6.8	6	11

Singapore depot

Item Description	Length (cm)	Width (cm)	Height (cm)
DB-1303	4.7	4.7	7.5
CAPECITABINE 500MG BU 12X	13.5	9	7
PACLITAXEL 30MG/5ML	3.8	3.9	7
Nab-PACLITAXEL 100MG	6	6.5	10.2

Germany depot

Item Description	Length (cm)	Width (cm)	Height (cm)
DB-1303	4.7	4.7	7.5
CAPECITABINE 500MG BU 12X	9.7	7.1	13.0
PACLITAXEL 30MG/5ML	5.9	5.9	7.4
Nab-PACLITAXEL 100MG	7.9	7.9	10.5

For Canada IPs

Item Description	Length (cm)	Width (cm)	Height (cm)
DB-1303	4.7	4.7	7.5
CAPECITABINE 500MG BU 12X	6.4	6.4	11.4
PACLITAXEL 100MG	4.4	4.4	8.9
Nab-PACLITAXEL 100MG	6.4	6.4	10.2

IP manager will confirm with the specific depot of receiving the request and ensure IP be shipped to the address site provides and the status in the RTSM be updated accordingly.

IP will be shipped using a validated shipping box with a temperature monitoring device to monitor the temperature throughout the shipment. The standard turnaround time for order dispatching from depot is three working days of receiving the order request.

General Remarks:

- Order request receives after 12pm, will be considered as orders received on the next business
- Day's timeline.
- For urgent orders that do not follow the standard timeline, additional charge is needed which needs to be approved by sponsor.
- If depot holiday falls on weekday, order request will be processed on the next business day.
- For Israel, the IPs shall be supplied with a Packing list/Proforma Invoice and a statement essentially stating that "The Study Drug has been released according to the MOH directive EX-012/01".
- All the documentation related to the IP must be retained as per local regulation requirement

Upon receipt of the supplies at the clinical site, the site staff will:

- Open the shipping container.

- Visually inspect the goods for signs of physical damage to the carton and to ensure that they are in good form (outer cartons need to be unsealed to inspect inner IP boxes, for inner boxes just ensure the seals are in place and no leakage is observed).
- Retrieve and stop the temperature monitoring device (see **Appendix 1**), download the data in pdf and file together with shipping documents. Upon completing this task hand over the device back to the courier personnel.
- If no temperature device alarm or damage occurred, IP should be immediately stored at the required temperature in its original carton until use. Once confirmed no temperature excursion occur, and the outer packing is intact and all drug shipping information is correct, the Pharmacist or designee need to confirm receipt of IP in the RTSM system.
- If an excursion or damage has occurred, site should immediately quarantine the affected IP on site at the required storage temperature of the IP and also quarantine the IP in the RSTM system and follow the section 4.4 reporting of temperature excursion or product complaints.
- All original receipt documentation for IP will be kept in the ISF at site for the entire duration of the study.
- DUALITY /delegate will ensure that sufficient quantities of the IP are supplied to the site. If at any time the site inventory levels are low, site staff need to initiate new order via the RTSM system for re-supply unless the inventory hits the minimal stock which will trigger an automatic drug supply.

4.3. IP Storage

- After the IP has been inspected, and deemed to be in good condition, it must be stored upright in a limited access temperature-controlled refrigerator in the site pharmacy. The area where the IP is stored must be a secure, monitored, locked environment with restricted access.
- Temperature requirement of each IP
- **DB-1303**
    - Stored at 2-8℃（36-46℉), protected from light, and vials must be kept in the outer carton until use to prevent light exposure. The IP can’t be frozen.
- **Paclitaxel**

  Canada
    - In original cartons at 20°C to 25°C (68°F to 77°F)
    - Retain in the original package to protect from light

  China
    - Protect from light, keep tightly closed
    - Below 25°C (It is stable at 15°C to 30°C)

  US
    - Follow drug package insert

  Rest of World
    - Does not require any special temperature storage conditions.
    - Keep the vial in the outer carton in order to protect from light

- **Capecitabine**

  Canada
    - At 20°C to 25°C (68°F to 77°F)
    - Excursions permitted to 15°C to 30°C (59°C to 86°F)
    - Keep tightly closed

  China
    - At 25°C
    - Permitted to 15°C to 30°C

- Out of reach of children

US

- Follow drug package insert

Rest of world

- Does not require any special storage conditions

- **Nab-paclitaxel**

Canada

- In original cartons at 20°C to 25°C (68°F to 77°F)

US

- Follow drug package insert

Rest of World

- Does not require any special temperature storage conditions. Suggest to store at 15°C to 30°C (59°C to 86°F)
- Keep the vial in the outer carton in order to protect from light

- The temperature of the pharmacy refrigerator storing the IP should be monitored at all times using a calibrated/validated device.
- Temperature monitoring logs (Site specific template or template developed by study team, See **Appendix 2**) must be maintained throughout the duration of the study until all IP are either returned to the Sponsor, expired or destroyed on site. All temperature logs must be available to the CRA for verification and copies must be filed within ISF upon archiving.
- IP storage excursions above or below the required temperature range must be reported to your CRA and then CRA reports to DUALITY immediately, please follow section 4.4.

4.4. Reporting of Temperature Excursions or Product Complaints

- If a temperature excursion (higher or lower than the required storage temperature) and/or product complaints occurs during storage at site or during transportation, delegated site staff must fill in the **TP-IMP-001-01 IP Deviation Report template** (See **Appendix 3**) and email the information to the CRA and include sponsor CMC representative (nancy.luo@dualitybiologics.com) in order to assess the impact of the temperature excursion and or product complaints on IP use. The email title should include the reason for the email, protocol number, the site number and, if a temperature deviation has been noted, 'ALARM'. For example, **Receipt confirmation and Temperature reading – Study xxx, Site# xxx – ALARM**. Any damage or other concerns noted should be added to the email as well. At the same time the pharmacist/delegate will need to place the IP into quarantine at the required storage temperature until further notice and quarantine the IP in the RTSM system (refer to RSTM manual for details).
- All fields in the form should be completed and there should be no blanks. If any field is not applicable, a line should be drawn through it, and NA written with initials and date.
- If it is possible, take a picture of the product defect and send along with the signed completed form.
- If the IP is assessed to be safe for use, written documentation from sponsor will be provided to the delegated site staff within 48 hours of awareness. The delegated site staff will then remove the IP from quarantine.
- If the IP is assessed and deemed to be unacceptable for use, written documentation will be emailed to the site. Site needs to assess whether a replacement IP order will be placed. DUALITY / delegate will notify site staff if the "unacceptable stock" should be returned to warehouse or destroyed at the site.
- All documentation and correspondence related to temperature excursions must be filed in the ISF.

4.5. IP Labelling Instructions

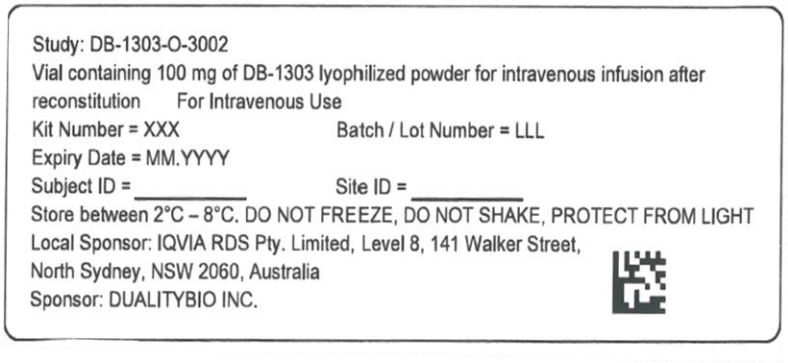
4.5.1 Bulk Labels

All IP labels, including labels affixed on cartons and inner boxes, comply with applicable local regulation requirements. Labels will, at a minimum, include the following information:

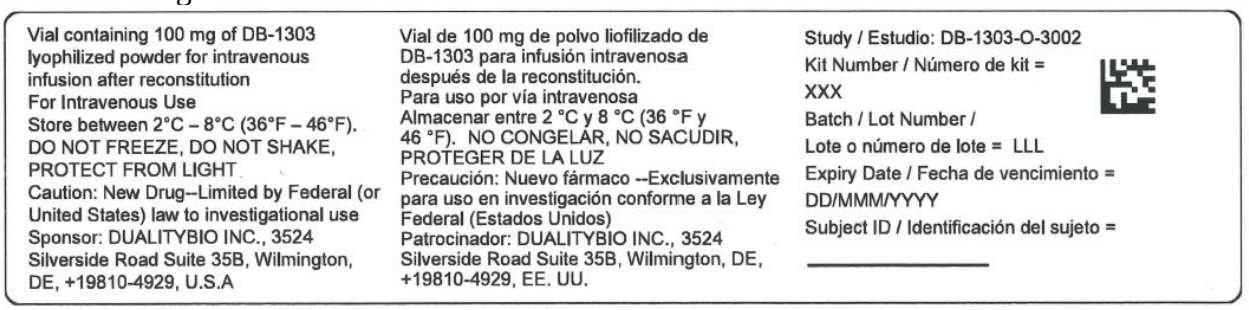
- Protocol Number
- Drug Name, strength / concentration and dosage form
- Quantity and the unit of measure
- Batch / lot Number
- Storage condition
- Re-test Date / expiry date
- Administration instructions
- Statement of "For clinical trial use only"
- Information of Sponsor

Sample images of each label are provided below.

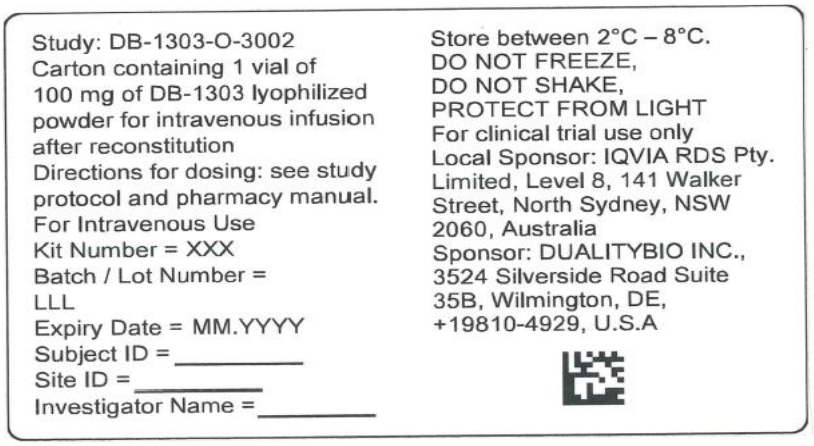
Vial label: DB1303 AUS Single Panel Label



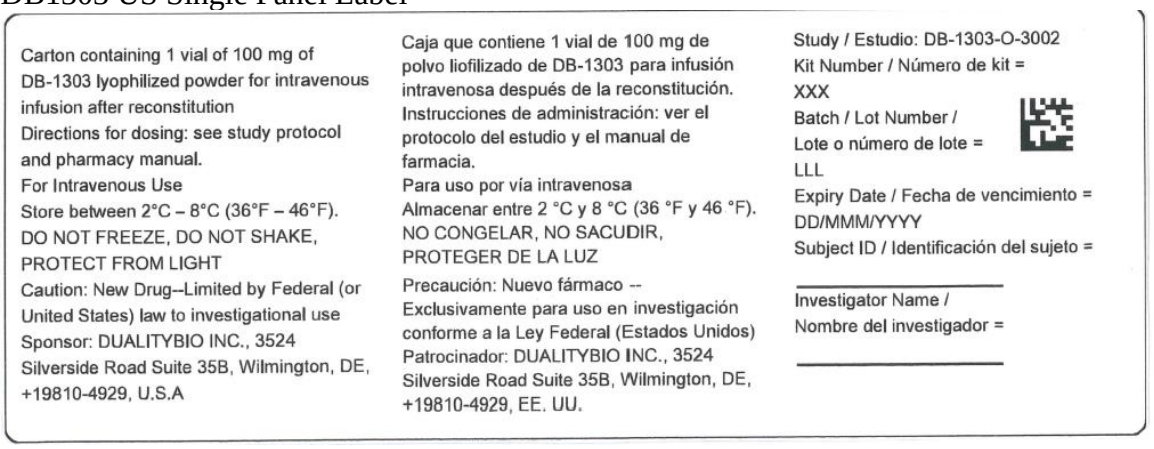
DB1303 US Single Panel Label



Carton label: DB1303 AUS Single Panel Label



DB1303 US Single Panel Label



4.5.2 Numbering of Vials

Individual vials will be numbered for this study. The rules for kit numbers are as follows.

- DB-1303: DXXXXXX (D with sequence number, starting from 000001)
- Paclitaxel: PXXXXXX (P with sequence number, starting from 000001)
- Capecitabine: CXXXXXX (C with sequence number, starting from 000001)
- Nab-paclitaxel: NXXXXXX (N with sequence number, starting from 000001)

Treatment for each subject visit will be prepared using the kits with the numbers from the RTSM system. Any remaining IP in the vial will be discarded. Any unused Capecitabine tablets will be returned to the site.

4.5.3 Dosing Containers

Infusion bags prepared for IP administration will be labelled according to the site's own SOP and in accordance with local regulatory requirements.

4.6. IP Dispensing

Site needs to log on the EDC system and enter the information (country, treatment, amount of the kits planned to be dispensed and dose level) in the drug dispensation page, then the kit numbers will be displayed in the drug dispensation page in the EDC system. Site will dispense the drug following the displayed kit numbers. There will be a system query when the selection of 'amount of kits planned to be dispensed' from the dropdown list is not consistent with the calculation by EDC automatically. You need to double check the amount of the kits and make correction as needed.

- Manually calculate the number of vials for DB1303

- Example: If a subject's weight is 80kg, the dose level is 8 mg/kg, the calculation method of the vials would be:

80 kg × 8 mg/kg = 640 mg
Considering the strength of DB-1303 is 100 mg/vial, the vials would be
640mg/(100mg/vial) =6.4 vials
Round up to 7 vials for drug dispensing.

4.7. IP Preparation and Administration

An individual subject's dose will be prepared in accordance with the protocol (as outlined below), the site pharmacy's SOP, and applicable laws and regulations. Please always refer to the re-test date on the labeled vial for usability.

If there's any broken or damaged vial during IP preparation, site should log on the RTSM system to manual dispense additional vial to replace the vial (details please refer to the RTSM manual).

4.7.1 IP Preparation

DB-1303

Dosage

- Dose level is 8mg/kg
- The subject's weight at screening will be used to calculate the initial dose. If, during the course of treatment, the subject's weight has changed by ≥ ± 10%, the subject's dose will be recalculated based on the subject's updated weight. However, sites can modify the dosage if the weight changes after screening and if the site's local practice is more conservative than the 10% threshold for dose adjustment (e.g., dose adjustment if 5% variance in the subject's weight).
- IP must be prescribed by the Investigator and documented in the source documents.

Preparation

- Reconstitute each 100 mg vial by using a sterile syringe with a 20-22 gauge needle to slowly inject 5 mL of Sterile Water for Injection, USP into each vial to obtain a final concentration of 20 mg/mL.
- Swirl the vial gently until completely dissolved.
- Do not shake product.
- The solution is clear and colorless to light yellow. Visually inspect the solution for particulate matter and discoloration. Do not use vial if the solution is cloudy and/or if there is pronounced discoloration and/or visible particles.
- Calculate the volume for dilution
    - Considering the final concentration is 20mg/mL, if the required dose is 640mg
      The volume would be 640/20=32mL
- The amount of solution extracted is calculated using rounding method and will not exceed 5% of the total dose. For safety reasons, it is recommended to round down the calculated volume. If the calculated value is 19.47ml, the extracted volume is recommended to be 19 ml or 19.4 ml depending on the syringe used during IV preparation.
- Withdraw calculated volume of reconstituted solution using a sterile syringe with a 20-22 gauge needle, and inject into a 100 mL or 250 mL IV bag containing D5W (Dextrose 5% in Water) and ensure the final drug concentration is 0.64 mg/mL to 12 mg/mL. 100 mL is preferred unless a subject's weight will make the concentration exceed 10mg/ml. Do not use Sodium Chloride Solution, USP. DB-1303 is compatible with an infusion bag made of non-PVC and PVC film. DB-1303 reconstituted solution can be alternatively transferred to IV bags by CSTD to avoid use of needle.

Site can follow its practice to prime the IV line with saline before connecting the IV bag.

- Gently invert the infusion bag to thoroughly mix the solution.
- Do not shake.
- Discard any unused portion left in the vial.
- After dilution if not used immediately, DB-1303 solution from beginning of reconstitution (vial puncture) till completion infusion should be within 4hours at room temperature or at 2-8°C for up to 24 hours. After reconstitution, if the DB-1303 solution exceeds 24hours, the unused portion should be discarded.

Paclitaxel

Dose level is 80 mg/m^2

- Paclitaxel injection must be diluted prior to infusion. Paclitaxel injection should be diluted in 0.9% Sodium Chloride Injection, USP; 5% Dextrose Injection, USP; 5% Dextrose and 0.9% Sodium Chloride Injection, USP; or 5% Dextrose in Ringer's Injection to a final concentration of 0.3 to 1.2 mg/mL. The solutions are physically and chemically stable for up to 27 hours at ambient temperature (approximately 25°C) and room lighting conditions. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit. Upon preparation, solutions may show haziness, which is attributed to the formulation vehicle. No significant losses in potency have been noted following simulated delivery of the solution through IV tubing containing an in-line (0.22 micron) filter.
- Data collected for the presence of the extractable plasticizer DEHP [di-(2-ethylhexyl) phthalate] show that levels increase with time and concentration when dilutions are prepared in PVC containers.
- Consequently, the use of plasticized PVC containers and administration sets is not recommended.
- Paclitaxel injection solutions should be prepared and stored in glass, polypropylene, or polyolefin containers. Non-PVC containing administration sets, such as those which are polyethylene-lined, should be used. Paclitaxel injection should be administered through an in-line filter with a microporous membrane not greater than 0.22 microns. Use of filter devices such as IVEX-2 filters which incorporate short inlet and outlet PVC-coated tubing has not resulted in significant leaching of DEHP. Site can follow its practice to prime the IV line with saline before connecting the IV bag.
- The Chemo Dispensing Pin™ device or similar devices with spikes should not be used with vials of paclitaxel injection since they can cause the stopper to collapse resulting in loss of sterile integrity of the paclitaxel injection solution.

Stability

- Upon refrigeration, components in the paclitaxel injection vial may precipitate, but will redissolve upon reaching room temperature with little or no agitation.
- There is no impact on product quality under these circumstances. If the solution remains cloudy or if an insoluble precipitate is noted, the vial should be discarded. Solutions for infusion prepared as recommended are stable at ambient temperature (approximately 25°C) and lighting conditions for up to 27 hours.

Capecitabine
Dose level is 1000 or 1250 mg/m^2

Nab-paclitaxel

Dose level is 100 mg/m^2

- Aseptically, reconstitute each vial by injecting 20 mL of 0.9% Sodium Chloride Injection, USP.
- Slowly inject the 20 mL of 0.9% Sodium Chloride Injection, USP, over a minimum of 1 minute, using the sterile syringe to direct the solution flow onto the INSIDE WALL OF THE VIAL.
- DO NOT INJECT the 0.9% Sodium Chloride Injection, USP, directly onto the lyophilized cake as this will result in foaming.
- Once the injection is complete, allow the vial to sit for a minimum of 5 minutes to ensure proper wetting of the lyophilized cake/powder.
- Gently swirl and/or invert the vial slowly for at least 2 minutes until complete dissolution of any cake/powder occurs. Avoid generation of foam.
- If foaming or clumping occurs, stand solution for at least 15 minutes until foam subsides.
- Each mL of the reconstituted formulation will contain 5 mg/mL paclitaxel.
- The reconstituted suspension should be milky and homogenous without visible particulates. If particulates or settling are visible, the vial should be gently inverted again to ensure complete resuspension prior to use. Discard the reconstituted suspension if precipitates are observed. Discard any unused portion.
- Calculate the exact total dosing volume of 5 mg/mL suspension required for the patient and slowly withdraw the dosing volume of the reconstituted suspension from the vial(s) into a syringe: Dosing volume (mL)=Total dose (mg)/5 (mg/mL).
- Inject the appropriate amount of reconstituted drug into an empty, sterile intravenous bag [plasticized polyvinyl chloride (PVC) containers, PVC or non-PVC type intravenous bag]. The use of specialized DEHP-free solution containers or administration sets is not necessary to prepare or administer Nab-Paclitaxel infusions. The use of medical devices containing silicone oil as a lubricant (i.e., syringes and intravenous bags) to reconstitute and administer Nab-Paclitaxel may result in the formation of proteinaceous strands.
- Visually inspect the reconstituted Nab-Paclitaxel suspension in the intravenous bag prior to administration. Discard the reconstituted suspension if proteinaceous strands, particulate matter, or discoloration are observed.

- **Stability of Reconstituted Suspension in the Vial**

- Reconstituted (starting from vial puncture) Nab-Paclitaxel in the vial should be used immediately, but may be refrigerated at 2°C to 8°C (36°F to 46°F) for a maximum of 24 hours if necessary. If not used immediately, each vial of reconstituted suspension should be replaced in the original carton to protect it from bright light. Discard any unused portion.

- **Stability of Reconstituted Suspension in the Infusion Bag**

- The suspension for infusion when prepared as recommended in an infusion bag should be used immediately, but may be refrigerated at 2°C to 8°C (36°F to 46°F) and protected from bright light for a maximum of 24 hours.
- The total combined refrigerated storage time of reconstituted Nab-Paclitaxel in the vial and in the infusion bag is 24 hours. This may be followed by storage in the infusion bag at ambient temperature (approximately 25°C) and lighting conditions for a maximum of 4 hours.

- **Discard any unused portion.**

4.7.2 IP Administration

DB-1303

- Attach the IV bag containing the DB-1303 solution to the infusion set, 0.2 or 0.22 or 0.5 µm

polyethersulfone (PES) in line filter, and infusion pump (such as, PE lined and FQ PES).

- Infusion set material can be either of PVC and non-PVC.
- Do not administer as an intravenous push or bolus.
- Do not mix DB-1303 with, or administer as an infusion with, other medicinal products.
- Follow site standards to flush the line with normal saline after infusion.
- The study results shown that good compatibility of DB-1303 in contact with closed system transfer devices (CSTDs).). DB-1303 IV bags can be alternatively connected with infusion set by CSTD.
- DB-1303 should be given via intravenous infusion over about 90 minutes for the first infusion and if the subject does not experience an infusion reaction, DB-1303 may be given as an approximately 30 to 60 minutes IV infusion for 100 mL D5W and as a 60-minute IV infusion for 250 mL D5W for subsequent cycles.
- In the unanticipated event that more than 250 mL D5W is required, a prolonged infusion time can be acceptable for subjects which require more than 250 mL D5W to meet the requirement of dilution; in this case, multiple 100 mL or 250 mL IV bags could be used, and for each IV bag it should not exceed 4 hours from the start of reconstitution to the end of infusion. If infusion is not needed immediately, the IV bags could be stored in 2-8°C fridge for no more than 24 hours. After reconstitution, if the DB-1303 solution exceeds 24 hours, the unused portion should be discarded.
- Prophylactic pre-medications should be used as per section 6.5.1 of the Protocol (Table 8).
- Management of adverse reactions may require temporary interruption, dose reduction, or treatment discontinuation. Refer to the protocol for further details.

Paclitaxel

- QW (Qua que Week) in 3-week cycles
- See more details in IP preparation section of Paclitaxel (section 4.7.1).

Capecitabine

Twice daily orally for 2 weeks followed by a 1-week rest period in 3-week cycles

- Round the recommended dosage for patients to the nearest 500 mg dose to provide whole Capecitabine tablets.
- Swallow Paclitaxel tablets whole with water within 30 minutes after a meal. Do not chew, cut, or crush Capecitabine tablets
- Take Capecitabine at the same time each day approximately 12 hours apart.
- Do not take an additional dose after vomiting and continue with the next scheduled dose.
- Do not take a missed dose and continue with the next scheduled dose.
- Capecitabine is a hazardous drug. Follow applicable special handling and disposal procedures.

Nab-paclitaxel

QW for 3 weeks followed by a one-week rest period in 4-week cycles. See more details in IP preparation section of Nab-Paclitaxel (section 4.7.1).

5. Administration Documentation

The following notation should always be included as part of source documentation for IP administration.

- Part of Preparation
    - Reconstitution start time (starting from puncture)
    - Temperature during transportation of the prepared IP if applicable
- Part of prescription

  - Study Number
  - Subject ID
  - Date of prescription
  - Dosing schedule
  - Total calculated dose

- Part of Administration Source
  - Total amount of IP administered
  - Start time
  - Stop time
  - Were there any interruptions
  - Temperature of storage when there's an interruption
  - Total volume administered
- Participant diary for Capecitabine

6. Accountability, IP Return and Destruction

In accordance with GCP, the site will account for all supplies of the IP. Details of receipt, storage, destruction, and return of the IP will be recorded according to site's SOPs. All used or expired IP will be destroyed by the site in accordance with the site's destruction SOP or consult sponsor if site cannot destroy. The box of each vial will be retained until the site CRA completes the accountability. All unused IP (including unused Capecitabine tablets patients return to site) will be returned or destroyed at the conclusion of the study or as per site request and as instructed by DUALITY or delegate, after drug accountability is completed. Depots for drug return and destruction are as below. Site/CRA needs to trigger the drug return and destruction request via the RTSM. The specific depot will arrange site pickup and courier upon receipt of the request within one week. Expired IP and unused IP can be handled via one shipment. For IPs to be returned and destroyed, no temperature control will be used during shipment. Depot should update the status of the drug return and destruction via the RTSM within 7 days of the IP is pickup. If not, RTSM system might trigger reminder emails.

<table>
<tr><th>Countries</th><th>Return & destruction depot</th><th>Email Address</th></tr>
<tr><td>China (Mainland)</td><td>STZ
Unit 4101, Building#4, No. 955 Shang Feng Road, Tangzhen, Shanghai 201210, China</td><td>Shanghai.ReturnRequests@catalent.com</td></tr>
<tr><td>Australia</td><td rowspan="3">Catalent CTS (Singapore) Pte. Ltd.
No. 1 Jalan Kilang #02-01/02
Singapore 159402
ATTN: SNG Returns Team</td><td rowspan="3">Singapore.ReturnsRequests@catalent.com</td></tr>
<tr><td>Hong Kong</td></tr>
<tr><td>South Korea</td></tr>
<tr><td>Belgium</td><td rowspan="6">MNX Global Logistics B.V.
Attn.: Return Handling Team
Maroastraat 26 1060 LG
Amsterdam
Netherlands</td><td rowspan="6">catalent.ams@mnx.com</td></tr>
<tr><td>France</td></tr>
<tr><td>Germany</td></tr>
<tr><td>Hungary</td></tr>
<tr><td>Poland</td></tr>
<tr><td>Spain</td></tr>
<tr><td>Italy</td><td>Alloga Italy
Corso Stati Uniti 9/A -
35127 Padova – Italy</td><td>clinicaltrial@alloga.it</td></tr>
</table>

Canada	Catalent Pharma Solutions- Return goods 10245 Hickman Mills Dr, Dock 10, Kansas City Missouri, 64137, United States	GMB-DC-KCMReturns@catalent.com
USA	Catalent Pharma Solutions- Return goods 10245 Hickman Mills Dr, Dock 10, Kansas City Missouri, 64137, United States	GMB-DC-KCMReturns@catalent.com
UK	Catalent Pharma Solutions 1 Inchwood Park, Bathgate, West Lothian, EH48 2FY, United Kingdom	GMB-DC-GBL-BTHReturnsDept@catalent.com
Turkey	SMO TU Lojistik Ve Ambalaj Sanayi Ve Ticaret Limited Şirketi I.A.O.S.B. 10053 Street, No: 7/1 Cigli/İzmir, Turkiye	depot-tr@oximio.com
Israel	Oximio-IL LTD. 6 Bareket Street Industrial Park North Caesarea 3079863 Israel	Depot-il@oximio.com

Appendix 1 Temperature Monitoring device Instruction

Temperature monitor instructic

Appendix 2 Temperature monitoring log

Site can use its own template. Each country can customize as per country requirement

DB-1303-O-300 2-%20%20%20Te

Appendix 3 TP-IMP-001-01 IP Deviation Report template

Site can use its own template. Each country can customize as per country requirement

TP-IMP-001%20I P%20Deviation%:

Appendix 4 Master IP accountability Log

Site can use its own template as long as it covers the basic information that study requires. Each country can customize as per country requirement. If site would like to use their own template the template needs to be reviewed and approved by the CRO.

DB-1303-O-300 2-%20Pharmacy%

DB-1303-O-300 2-%20Pharmacy%

DB-1303-O-300 2-%20Pharmacy%

DB-1303-O-300 2-%20Pharmacy%

Appendix 5 Subject level IP accountability log

Site can use its own template as long as it covers the basic information that study requires. Each country can customize as per country requirement. If site would like to use their own template the template needs to be reviewed and approved by the CRO.

DB-1303-O-300 2%20Subject%20

DB-1303-O-300 2%20Subject%20

DB-1303-O-300 2%20Subject%20

DB-1303-O-300 2%20Subject%20

Appendix 6 Participant Diary

DB-1303-O-300 2_Participant%20