Pharmacy Technical Review Form for CTIMPs

Note to Sponsors and Applicants:

This is a completed exemplar of the Pharmacy Technical Review Form. It is intended to be used as guidance by sponsors and applicants who are submitting a study to Pharmacy Assurance. It shows the information requirements and level of detail that the HRA registered pharmacy reviewer will need from to complete all the answers within the form and enable Pharmacy Assurance to be issued.

Please ensure that your study documentation provides enough detail to enable the reviewer to complete their review. It is not essential to submit a Pharmacy Manual. Where information is missing in your study documentation and is required to complete the review, please submit this in your covering email when you submit to Pharmacy Assurance.

Please note that Pharmacy Assurance will be provided based on the study documents listed in Section 2. Amendments will not be reviewed through Pharmacy Assurance.

Part 1: Study and reviewer identification. To be completed by lead nation administrative support (All nations)

Section 1: Study identification

Pharmacy Specialisms	Adult Oncology ☒ Paediatric Oncology ☐ Adult Non-oncology ☐ Paediatric Non-oncology ☐ Radiopharmacy ☐ ATIMPs ☐
Full Protocol Title	A Phase 2 trial of BVP953 in previously treated patients with metastatic stomach cancer.
Study Acronym (if applicable)	N/A
Sponsor Protocol Reference	BVP953
NRS ID Number (Scotland only)	1234
EudraCT Number	1234-123456-12
IRAS Number	123456
Sponsor Organisation	A Commercial Sponsor

Section 2: Documents reviewed as part of this submission

Document	Version Number	Date
Protocol	1.0	01 June 2018
Investigator's Brochure	1.1	01 January 2018
Pharmacy Manual	1.0	01 June 2018
Product labels	1.0	01 June 2018
Material Safety Data Sheet	1.1	01 June 2018

Section 3: Details of Sites

Number of sites in UK at initial submission	6
Total recruitment planned in UK at initial submission	25
Does the study involve Primary Care?	No

Part 2: Technical pharmacy review. To be completed by HRA Pharmacy Reviewer/Reviewers (All nations)

Section 4: Study Summary

a) Description of study treatment regimen Brief summary to be used as a reference, include full information on doses, routes of administration, timing of administration, length of infusion (if applicable), blinding and placebos	BVP953 at 20mg/kg as a single 30 minute intravenous infusion. Each 3-week treatment cycle will consist of a single dose on Day 1, followed by a rest period of 20 days.

Section 5: Pharmacy Resources

a) Type of Study	Dispensary ☐ Aseptic ☒ Radiopharmacy ☐
Set up, management and close-down costs	
a) Set Up/Close Down type	Type A ☐ Type B ☒ Type C ☐ Type D ☐
Additional resource information	

a) Dispensing schedule Include number of dispensing and frequency	Approximately 18 i.e. every 3 weeks up to 1 year
b) Duration of treatment E.g. 13 days/6 cycles/2 years/until disease progression	Up to 1 year, or disease progression or unacceptable toxicity, whichever occurs first.
c) Does the protocol dictate dispensing out of hours?	Yes ☐ No ☒

Section 6: Treatment allocation/Randomisation/Blinding

a) Is Pharmacy blinded?	Yes ☐ No ☒ N/A ☐
b) If local pharmacies will be involved in repackaging and/or relabelling open-label medication to blind, give details	N/A
c) Will Pharmacy be involved in treatment allocation?	Yes ☒ No ☐ N/A ☐
d) How will Pharmacy be notified of treatment allocation details?	Pharmacy team accesses IXRS system Pharmacy staff will allocate vials on IXRS.

e) Can randomisation be done in advance of patient visit?	No
f) Does dispensing need to be verified on IXRS by Pharmacy, and if so does it need to be done in real time?	Yes ☒ No ☐ N/A ☐
g) Can Pharmacy dispense from the IXRS system in advance of patient visits? If yes, specify the timescale for this.	Yes ☐ No ☒ N/A ☐

Section 7: Emergency Unbinding

a) What is the process for emergency unblinding?	N/A
b) Will Pharmacy be involved in emergency unblinding?	Yes ☐ No ☐ N/A ☒

Section 8: General Funding

a) Are there likely to be excess treatment costs or other local funding implications?	Protocol states that patients at risk from tumour lysis syndrome should be treated with rasburicase. The sponsor has confirmed that this will not be supplied or funded by them and must be sourced and funded from local hospital supplies.

b) Where product/products are not supplied free of charge, are they supplied at a discounted rate for the duration of the trial?	Yes ☐ No ☒
c) Is information given on compassionate use/ongoing supply after the trial finishes? Include arrangement details and whether there is written confirmation of the exit strategy.	Yes ☐ No ☐ N/A ☒ Maximum treatment duration is 1 year. No further treatment is permitted after this.
d) Other/Comments	None

Section 9: Further Information on Study

a) Method/methods permitted for calculating BSA (body surface area)	N/A ☒ Du Bois ☐ Mosteller ☐ Local practice ☐ Other (please specify) ☐
b) Method permitted for calculating dose based on weight	N/A ☐ IBW ☐ ABW ☒ Weight must be checked up to 24 hours ahead of each dose. Dose must only be changed after cycle 1 if there is > 10% change from initial weight.
c) Are methods permitted for calculating BSA/weight detailed in the protocol?	N/A ☐ Yes ☒ No ☐

d) Method/methods permitted for calculating GFR (glomerular filtration rate)	N/A ☐ Cockcroft-Gault ☒ Local practice ☐ Other (please specify) ☐
e) Blood test validity periods/Frequency specified	Blood tests can be taken up to 24 hours ahead of day 1 of each cycle.

Section 10.1: Product Information

Description and Product Type	
a) Description of Product Include name, strength, concentration, volume, form e.g. Drug A 100mg in 5ml Injection (10ml vial)	BVP953 freeze dried powder for concentrate for solution for infusion 45mg per 5ml vial. Diluted with 4.5ml WFI to make final concentration of 10mg/ml.
b) Is the product an IMP (investigational medicinal product) or AMP (auxiliary medicinal product)?	IMP ☒ AMP ☐
c) Are all the drug names correct (i.e. rINN)?	Yes ☒ No ☐
d) Route of administration (include detail of timing in relation to food and how to take etc.)	Intravenous
e) Licence status	Unlicensed

f) Properties of product requiring special attention	N/A ☐ Cytotoxic ☒ Monoclonal Antibody ☐ Cytotoxic Monoclonal Antibody ☐ Cytostatic ☐ Biological ☐ ATMP ☐ Radiopharmaceutical ☐ Other (please specify) ☐
g) Is it a controlled drug? If yes, include details of Sponsor's arrangements for safe and secure handling of drug	Yes ☐ No ☒ N/A ☐
h) If it is a controlled drug, which schedule is it in?	N/A ☒ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐
i) Will additional licenses be required?	Yes ☐ No ☐ N/A ☒
Dose banding and capping	
a) Is dose banding permitted? If nationally dose banded drug, is the use of national dose banding table permitted?	Yes ☐ No ☒ N/A ☐

b) What dose capping/rounding protocols are permitted?	The calculation to find the mg required is based on the weight of the patient and must be followed to provide the correct volume of solution required for infusion. Once the mg have been calculated the sponsor has stated it would be acceptable to round the volume to the nearest 0.5ml, as syringes will not be accurate to anything less – see email confirmation from sponsor. There are no dose capping protocols in place.
Product Source	
a) Source of product	Supplied by sponsor
b) If the product is to be sourced from commercial stocks, will it be reimbursed?	Yes ☐ No ☐ N/A ☒
c) If the product is to be sourced from commercial stocks, can any brand be used?	Yes ☐ No ☐ N/A ☒
d) Is the use of pre-filled infusion bags and/or syringes procured through a third-party manufacturer permitted?	Yes ☐ No ☐ N/A ☒
Packaging and Storage	

a) Packaging of IMP E.g. Primary: in HDPE bottles with child resistant cap; Secondary: 1 carton (kit) contains 2 bottles. Dimensions: Kit dimensions – 12x20x10cm	15 vials per box kit. Kit dimensions are: 20.3 x 13.1 x 6.2cm.
b) Storage conditions of the product E.g. 2-8°C. Include details of temperature monitoring requirements and temperature deviation procedures	2-8°C. Temperature records will be checked at each monitoring visit. In the event of a temperature deviation, the vials must be placed into quarantine and the sponsor contacted within 24 hours of the deviation being recorded. The vials must also be quarantined in IXRS by pharmacy staff.
c) Storage space requirements for initial supplies i.e. details on size of initial shipment	Initial supply to site is 75 vials = 5 kits. Quantity of stock held at site will then depend on recruitment level. NOTE: Due to kit size and number of vials required for each dose e.g. a 70kg patient will require 31 vials (2+ kits) fridge storage space may be an issue.
Product Preparation	
a) Provide detailed information on methods of reconstitution/dilution/preparation Include information on diluents, time to dissolve/reconstitute, container compatibility, equipment (filters etc.) and safety handling requirements, detail on any drug/drug compatibility	Allow vials to equilibrate to room temperature for 20 minutes. Reconstitute each vial with 4.5ml WFI, avoiding foaming, to achieve a 10mg/ml solution. Once vials have been reconstituted, allow to stand undisturbed for 20 minutes to allow bubbles to disperse. The equivalent volume must be removed from a 250ml Sodium Chloride 0.9% non-PVC infusion bag before the dose is then added to it. Invert the infusion bag gently to mix. Filters must not be used during the preparation or infusion process.

b) Does the Sponsor require product preparation in an aseptically controlled environment, or can it be prepared using aseptic manipulation in a general area?	BVP953 must be prepared in an aseptically controlled environment.
c) Stability and storage requirements of reconstituted/diluted/prepared product of those requiring aseptic manipulation E.g. Diluted solution to be stored at room temperature for no more than 12 hours after preparation	After reconstitution: use as soon as manufacturing process allows. Maximum storage: 24 hours at 2-8°C. After dilution: use as soon as possible. Maximum storage: 72 hours at 15-25°C.
d) Are all drug formulations appropriate to the patient population (e.g. liquids for paediatrics)?	Yes ☒ No ☐
IMP/AMP Labelling	
a) Are the drug labels available for review?	Yes ☒ No ☐ N/A ☐
b) For IMP/IMPs, are these compliant with Annexe 13?	Yes ☒ No ☐
c) Is there any other information that should be on the labels?	No

d) Are sites allowed to use their own labels in their local format?	Yes ☒ No ☐
e) Are sites required or permitted to add their own dispensing labels?	Yes ☒ No ☐
f) Is there consistency between drug names in the protocol and on the label?	Yes ☒ No ☐
Management of IMP/AMP	
a) Will the Sponsor provide prescription forms or is it permitted for sites to use their own? If it is permitted for a site to use their own, will the Sponsor need to approve the prescription forms?	Sites may use their own prescription forms.
b) Accountability requirements Check if site's own accountability logs may be used	Sites must use the sponsor's accountability log, which is a single combined patient and inventory log. It is also the responsibility of the pharmacy department to maintain the inventory of stock in IXRS by allocating vials at each visit, recording shipment receipts and quarantining stock when necessary.
c) How will receipt and re-ordering of IMP/AMP be done?	Electronic (e.g. IXRS) As above, it is important that pharmacy ensures that stock levels are correct in IXRS so that automatic orders will be triggered when stock levels fall below the level set for each site.

d) How is the IMP transported from supplier to site? E.g. use of TempTale® device, requirement to return shipping box on receipt. Include any specific requirements for transportation of IMP from pharmacy to clinic on site	Each shipment will contain a Libero temperature monitoring device which must be downloaded immediately on receipt. The downloaded information should be uploaded to the IXRS to confirm receipt and also printed and retained in the pharmacy site file. Temperature deviations during transportation will trigger an alert in IXRS. In this event the stock must be quarantined and the pharmacy department will be contacted by the sponsor with further instructions.
e) When will the initial shipment of IMP be sent? E.g. at site activation, at first patient screening, at first patient randomisation	At first patient screening.
f) What is the lead time for delivery of IMP to site once the order is placed?	Once an order is triggered in IXRS, pharmacy will receive notification by email. Pharmacy can also check if an order is in progress by logging in to IXRS. The lead time for delivery once an order is triggered is 48 hours.
g) Level of control required on trial stock E.g. dispensing of specific pack numbers, reporting stock balance	After each infusion is complete, pharmacy staff must access IXRS to verify that the number of allocated vials have been used. The sponsor has also requested that sites perform a weekly inventory check on IXRS to ensure that stock levels are correct.
h) Management of returned IMP Would pharmacy be responsible for a compliance count?	N/A

i) Disposal arrangements	Local disposal or return to sponsor Due to the cytotoxic nature of BVP953, the sponsor prefers to have all drug destroyed locally. To facilitate this, a copy of the site's SOPs for local destruction of drug will be collected during the site initiation visit or monitoring visit to verify that a site may perform this activity. Any partially used vials or diluted dosing solutions of BVP953 should be disposed of in accordance with the site's standard drug disposal procedures. Any unused kits requiring destruction will need to be verified by the sponsor at a site monitoring visit prior to destruction. The site must provide written confirmation that study drug destruction has occurred on site and update IXRS accordingly. If the site is unable to destroy study drug locally, they must contact the sponsor to arrange study drug return.

Section 11: Additional Information

For example, information on supportive care (pre or post medication requirements), specific consumables, potential issue e.g. gene therapy isolators, or any further requirements (drug interactions/contraindications, concomitant meds) which may affect pharmacy. Please include details if the study is a stratified CTIMP or additional arms are expected.
As noted in section 8a above, sites should check local funding options for rasburicase. Sites should also be aware of fridge storage requirements, as noted in section 10.1 (packaging and storage, c).

Part 3: Nation specific review. To be completed by Pharmacy Reviewer/Reviewers (Devolved Administrations only, if applicable)

Section 12: Clinical Information

a) Is appropriate guidance given of support/rescue medication e.g. antiemetics/pre-medications?	Yes ☒ No ☐ N/A ☐
b) Is information given on side-effects?	Yes ☒ No ☐ N/A ☐
c) Is information given on treatment of side-effects?	Yes ☒ No ☐ N/A ☐
d) Are cautions/contra-indications listed?	Yes ☒ No ☐ N/A ☐
e) Is information given on concomitant medication permitted/prohibited?	Yes ☒ No ☐ N/A ☐
f) Is appropriate information given on dose modifications/delays and interruptions?	Yes ☒ No ☐ N/A ☐
g) Is the drug information contained in the Participant Information Sheet complete and appropriate?	Yes ☒ No ☐ N/A ☐

h) Other/Comments	None

Section 13: GP Letter

a) Does the GP letter contain information regarding permitted/disallowed concomitant medications?	Yes ☒ No ☐ N/A ☐
b) Does the GP letter contain information regarding potential interactions and known side-effects as detailed in the study protocol?	Yes ☒ No ☐ N/A ☐
c) Is the GP required to see the patient in direct respect of their participation in the study? If yes – add detail.	Yes ☐ No ☒ N/A ☐
d) Is the GP required to prescribe any IMP or supportive medication as a result of patient participation in the study? If yes, add detail.	Yes ☐ No ☒ N/A ☐
e) Is the letter explicit on any GP activity required as a result of the patient's participation in the study? If yes – add detail	Yes ☐ No ☐ N/A ☒

Section 14: Commercial Costing Template/Fees Agreed

a) State version of commercial template used.	Version April 2019
Set up, management and close-down costs	
a) Set Up/Close Down for each additional site	Yes ☒ No ☐ N/A ☐
b) IMP management fee	Yes ☒ No ☐ N/A ☐
Per Patient Costs Per Drug	
a) Number of drugs:	Standard Dispensing 0 Aseptic Dispensing 1
b) Dispensing time for standard agent or IMP/AMP (excluding use of IVR/IWR)	Yes ☐ No ☒ N/A ☐
c) Aseptic dispensing agent time	Yes ☒ No ☐ N/A ☐
d) Controlled drug – additional dispensing time	Yes ☐ No ☒ N/A ☐
e) Use of IVR/IWR system for dispensing by Pharmacy (additional time)	Yes ☒ No ☐ N/A ☐

f) Pharmacy arrangement of IMP delivery or posting preparation time	Yes ☐ No ☐ N/A ☒
g) Patient drug accountability time/medicine reconciliation	Yes ☒ No ☐ N/A ☐
Variable Costs (only charged if applicable)	
a) Storage space over 0.5m² approx. (=one shelf 0.3m deep x 1.5m long) per month	Yes ☒ No ☐ N/A ☐
b) Waste disposal as hazardous waste per 50L container	Yes ☒ No ☐ N/A ☐
c) Waste disposal storage pending collection or disposal of all unused/unwanted/expired medicines originally supplied by Sponsor per month or part thereof (Chargeable only if not collected within 1 month of the first request to collect)	Yes ☒ No ☐ N/A ☐
Additional costs (to be met by Sponsor as required)	
a) Re-labelling and releasing of IMP batch (e.g. shelf life extension)	Yes ☒ No ☐ N/A ☐

b) CRA-requested dedicated Pharmacy staff time to support monitoring visits. Chargeable as additional to standard/routine service provision of basic access, hospitality, documentation provision and query response	Yes ☒ No ☐ N/A ☐
c) Revision of relevant SOPs or IMP documentation as a result of a substantial protocol amendment	Yes ☒ No ☐ N/A ☐
d) Non-standard reporting of or additional company requested stock or temperature checks	Yes ☒ No ☐ N/A ☐
Miscellaneous Costs	
a) IMP specific consumables (total cost)	Yes ☐ No ☒ N/A ☐
b) Equipment purchase for specific IMP requirements in storage space or conditions (total cost)	Yes ☐ No ☒ N/A ☐
Drug Costs	
a) Name of drug/product	BVP953

b) Drug reimbursement to be covered in contract	Yes ☐ No ☐ N/A ☒
Potential Fees that would be specific to individual sites and their agreement to commit to extra workload	
a) Courier/posting costs for IMPs (third party costs as required e.g. per patient)	Yes ☐ No ☐ N/A ☒
b) Out-of-hours working (Usual staff hourly rate + 100%)	Yes ☒ No ☐ N/A ☐
c) Extending working hours (Usual staff hourly rate + 50%)	Yes ☒ No ☐ N/A ☐
d) Other/Comments	None

Section 15: Non-commercial costing

a) Are fees available for any activities relating to the placebo drug in the project?	Yes ☐ No ☐ N/A ☒
b) Other/Comments	None

Section 16: General

a) Any comments on study design?	None
b) Are the archiving arrangements specified?	Yes ☒ No ☐ N/A ☐
c) Other/Comments	None

Section 17: Identified Sites

List all Potential Sites	Local Pharmacy Contact	Contact Made
An Oncology Centre, Scotland	A Pharmacist 1	Yes ☒ No ☐ N/A ☐
An Oncology Centre, Northern Ireland	A Pharmacist 2	Yes ☒ No ☐ N/A ☐
An Oncology Centre, England	A Pharmacist 3	Yes ☐ No ☒ N/A ☐
		Yes ☐ No ☐ N/A ☐
		Yes ☐ No ☐ N/A ☐

Part 4: Review outcome. To be completed by HRA Pharmacy Reviewer/Reviewers (All nations)

Section 18: Review form completion

Completed By (Lead Reviewer)	Employing Organisation/Health Board	HRA registered reviewer number	Date	Outcome
A Pharmacist	A Trust/Health Board NHS Scotland/Northern Ireland	HRA1111PA	10 December 2019	1 ☐ 2 ☒ Check funding options for rasburicase and also fridge storage space.

Outcome

1 **Coordinated Review Completed** All risks managed & mitigated. Proceed to final local review

2 **Coordinated Review Completed** Some risks require local mitigation. Proceed to local review with clarification required

Completed By (Additional Reviewer)	Employing Organisation/Health Board	HRA registered reviewer number	Date
N/A	N/A	N/A	N/A