Mock IMPD for an over-encapsulated EU licensed medicinal product and a placebo to match

S DRUG SUBSTANCE
Not applicable.

P INVESTIGATIONAL MEDICINAL PRODUCT UNDER TEST
P.1 Description and Composition of the Investigational Medicinal Product:
The IMP is an over-encapsulated Wonderdrug 5mg Tablet (Drugs-R-Us, PL 98765/0001). The composition of the product is outlined below:

Component	Reference	Amount
Wonderdrug 5mg Tablet	PL 98765/0001	1
Lactose (back-fill)	Ph. Eur.	q.s.
Gelatin Capsule (Swedish Orange, size 00)	Supplier's CoA	1

P.2 Pharmaceutical Development:
Encapsulation of the Wonderdrug 5mg Tablets is not expected to have any significant effect on the dissolution profile of the drug product. The active substance (Wondersubstance) is freely soluble in aqueous media and previous studies have shown that the gelatin capsule will disintegrate within 5 minutes. For this reason comparative dissolution testing between the encapsulated and non-encapsulated tablets has not been conducted.

Lactose has been chosen to back-fill the capsules. Compatibility of this excipient with the tablet is not a concern since lactose is already present in the formulation for the licensed product (see SmPC).

The over-encapsulated tablets will be packaged in HDPE containers. This is the same container closure system as for the marketed product.

P.3 Manufacture:
P.3.1 Manufacturer(s)
Manufacture, packaging and labelling of the over-encapsulated Wonderdrug 5mg Tablets is carried out by:

Hospital Manufacturing Limited
Hospital Way
Anytown
Anywhere
UK

A copy of the MA(IMP) has been included as part of this submission.

P.3.2 Batch Formula
It is expected that a batch of 1000 capsules will be manufactured. *(Given the simple composition a batch formula has not been included)*

P.3.3 Description of Manufacturing Process and Process Controls
One intact Wonderdrug 5mg Tablet is placed inside a capsule shell by hand, back-filled with lactose and closed. The capsules are visually inspected and packed into HDPE bottles.

P.4 Control of Excipients:
P.4.1 Specifications
The lactose complies with the current edition of the Ph. Eur.
The gelatin capsule is non-compendial. This will be sourced from CapsuCompany and will meet the specification provided below:

Composition of Swedish orange gelatin capsules

Component	Quantity (% w/w)
Iron oxide	1.1817 %
Titanium dioxide	0.4916 %
Gelatin	qs 100%

Specification for Swedish orange gelatin capsules

Test	Acceptance Criteria	Method
Appearance	2-piece, Swedish orange opaque cap/body, unmarked hard gelatin capsule	Visual
Identification of Gelatin Test A Test B	 A yellow precipitate is formed. Turbidity is produced	Methods provided by vendor (modified USNF Monograph for Gelatin)
Capsule Weight Weigh at least 30 capsules individually.	±10% of target weight	Method provided by vendor
Loss on Drying	13.0 – 16.0% of its weight	Method provided by the vendor (modified USP <731>)
Microbial Limits Test Total aerobic microbial count Total combined mould and yeast count Absence of Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli, and Salmonella species.	 Not more than 1000 CFU/g Not more than 100 CFU/g Absent	 USP <61> or Ph. Eur. 2.6.12 & 2.6.13

P.4.5 Excipients of Animal or Human Origin
The gelatin and lactose are of animal origin.

P.5 Control of the Investigational Medicinal Product:
P.5.1 Specifications

	Acceptance criteria	**Method**
Appearance	Size 00 red capsule containing one intact tablet marked 'WD/5'and a fine white powder	Visual inspection

P.5.2 Analytical Procedures
The capsules are examined for conformance of colour and shape. The contents are tipped out and examined against a white background

P.5.3 Validation of Analytical Procedures
Not applicable.

P.5.4 Batch Analyses
Manufacture of the drug product has not yet been completed; however, given the simple manufacturing process and specification it is proposed not to provide batch analysis data.

P.7 Container Closure System:
The capsules will be packed in HDPE bottles with polypropylene closures.

P.8 Stability:
The shelf life for the marketed Wonderdrug product is 36 months when stored below 25 degrees C in HDPE bottles. It is proposed to assign a shelf life of 12 months to the over-encapsulated tablets, given that the modification is not likely to have an impact on the stability of the input product and given that the storage container is the same as that used for the marketed product. The expiry date for the over-encapsulated product will not exceed that of the input marketed product.

PLACEBO TO OVER-ENCAPSULATED WONDERDRUG TABLETS

Description and Composition
The placebo is a Swedish Orange size 00 capsule containing Lactose Ph. Eur.

Component	**Reference**	**Amount**
Lactose	Ph. Eur. (current)	q.s.
Gelatin Capsule (Swedish	Supplier's CoA	1

Orange, size 00)		

Manufacturer(s)
The placebo product is manufactured, packaged and labelled by:
Hospital Manufacturing Limited
Hospital Way
Anytown
Anywhere
UK

Description of Manufacturing Process and Process Controls
A capsule shell is packed with lactose and closed. The capsules are visually inspected and packed into HDPE bottles.

Control of Excipients:
As for the active product

Control of the Investigational Medicinal Product:
Specifications

	Acceptance criteria	**Method**
Appearance	Size 00 red capsule containing a fine white powder	Visual inspection

Analytical Procedures
The capsules are examined for conformance of colour and shape. The contents are tipped out and examined against a white background

Validation of Analytical Procedures
Not applicable.

Batch Analyses
Manufacture of the placebo product has not yet been completed; however, given the simple manufacturing process and specification it is proposed not to provide batch analysis data.

Container Closure System:
The capsules will be packed in HDPE bottles with polypropylene closures.

Stability:
A shelf life of 12 months to cover the anticipated duration of the clinical trial is proposed. This will not exceed the shelf life of the input raw material.

Appendicies
A1. Adventitious Agents Safety Evaluation

Non-viral adventitious agents
The lactose for use in the manufacture of the IMP will be obtained from milk sourced from healthy animals in the same conditions as milk collected for human consumption and no other ruminant materials (except calf rennet) are used in its preparation.

The EDQM Certificate of Suitability numbers under which the gelatin capsules are manufactured are provided below:
Rx-CEP xxxx-xxx
Rx-CEP xxxx-xxx
Rx-CEP xxxx-xxx