INSTRUCTIONS FOR THE PREPARATION OF ABSTRACTS SUBMITTED ON-LINE

On-line Submission

Abstracts should be prepared by using a Word template downloaded from the BPS website at http://www.bps.ac.uk Once downloaded and completed the template and any other accompanying image or data which cannot be inserted into the template must be uploaded via the website. Once you have prepared your abstract you will need to fill in a brief on-line form giving your details. Indicate your preferred method of presentation and the relevant category and keywords for your abstract. Keywords will not be printed but will be used for indexing *If you are not a full BPS member give the name of the member who will introduce the abstract or alternatively contact Dr Simon Maxwell, Vice President-Clinical via the BPS office (email: lvh@bps.ac.uk).* The process is simple and swift. You will receive an e-mail acknowledgment with a reference number and a BPS contact for any queries.

Abstract Template (see example on page 4)

Text can only be inserted in the form areas (greyed) in the template. The size of the abstract will be reduced by 25% when it appears in the abstract book and the Proceedings Supplement. It should therefore be word-processed using the font set in the template document (Times New Roman 12). Document settings must not be changed, as an abstract may be made unsuitable for reproduction or the abstract may not be accepted at the Meeting on the grounds that it is illegible.

Please make sure you type your title in the top box removing the existing text. The title should occupy no more than two lines and contain no more than 160 upper case characters, including spaces. Affiliations should be noted at the top of the left hand column and not in the same cell as the title.

The abstract template has a two-column format with a space between columns of 1 cm. Tables should be printed in single column width. Do not use vertical lines between columns in tables. When a figure or table is included, it should be referred to in the text as Figure 1 or Table 1. Single spacing should be used, except between paragraphs which should have 1.5-line spacing. Paragraphs should not be indented. Bold type should not be used.

The abstract document will be used untouched (except for the insertion of a number) for reproduction in the pre-circulated abstract book and the Proceedings Supplement of the Journal. Abstracts not conforming to the required standards of word processing or of style will be returned for resubmission at a subsequent meeting.

General

At least one author must be a member of the Society; if none of the authors is a member, the abstract must be 'introduced' by a member, whose name should appear (in brackets) after the names of the authors. A member may introduce any number of abstracts, but should include an order of priority in case the meeting is oversubscribed. Abstracts submitted by student members must also be introduced by a full member. Abstracts are accepted on the understanding that they have any necessary internal approval. Studies involving human subjects are assumed to have been approved by the Ethics Committee of the investigator's institution.

Abstracts should start with an introduction and, where appropriate, a statement of the aims of the work followed by methods, results (in the form of experimental data) and end with a conclusion and references. Where animals are used, the species, strain, sex and weight range should be given. Details of statistical analysis, n numbers and means and estimate of variability should be quoted where relevant. The use of novel acronyms and numbers for compounds should be avoided unless a reference or structure is provided.

References in the text should follow a standard style: either 'Jones (1990) reported' or, after a statement '(Jones, 1990;Brown *et al*., 1990)'. Use *et al.* for more than one name. References should be listed in alphabetical order at the end of the text, omitting the titles. In multiple author references, the number of names should be limited to one and '*et al.*' inserted where necessary.

For oral communications, the first-named author indicates the one who intends to present the work. Use other symbols or numerals as superscripts to indicate other affiliations.

At the meeting, the Society will expect the presentation to comply with the abstract contents and there will be a formal vote on acceptance for publication. Abstracts are accepted on the understanding that they have not been published elsewhere and are not 'in press' in a fuller form.

Any queries should be directed to jmc@bps.ac.uk or to BPS Office, 16 Angel Gate, City Road, London, EC1V 2SG, UK. Tel. 44 (0)20 7417 0111

BRITISH **P**HARMACOLOGICAL **S**OCIETY MEETINGS

General Guidelines for the Preparation of Abstracts

The Society has a commitment to excellence in the content and presentation of work at its scientific meetings and to the publication of abstracts that reflect the quality of the work of its members and guests.

To avoid abstracts being referred or rejected, it is essential that abstracts intended for publication should be in the correct format.

The text should state unambiguously the aims to be fulfilled, how and what data were actually obtained and in which respect these may contribute significantly to the relevant topic.

Aims of the work being presented and the reasons for undertaking the study must be stated clearly.

Methods must be given in sufficient detail to allow assessment of their appropriateness. Details should either be given in the text or be contained within a cited reference, which must be a paper (not another abstract) already in print or accepted for publication. Include the number of subjects or experimental animals (species stated), solutions used, doses or concentrations of drugs (including the identification of drugs mentioned by code number), whether or not anaesthesia was used (and, if so, what type) and methods of recording of responses or collection of data.

Results section must contain the authors' own original, unpublished data (with s.d. or s.e.m.), supported by statistical analysis where appropriate. Mere descriptions of changes in easily quantifiable parameters will not be acceptable (see *Examples of Unacceptable Styles*). A table or legible figure may be used.

The abstract should end with a conclusion and references. In general, the abstract should be informative and contain as much detail as possible: phrases such as "will be presented" or "will be discussed" are not acceptable.

In order to provide evidence of "quality control" and to convince the reader of the significance of the observations, the raw data should be given, whenever possible; the number of experiments of each type must be indicated.

Examples of Unacceptable Styles

It is **unacceptable** to describe drug-induced effects solely in a qualitative manner, e.g. *the heart rate fell; the rise in blood pressure was greatly attenuated; the contractions were markedly reduced or abolished; the binding of ABZ 273043 was significantly inhibited or virtually eliminated; the rank order of potency was X>Y>Z; the response was not potentiated; an inhibition was usually seen.* It is **insufficient** simply to state that *there was* (or *was not*) *a significant change.*

Where it is not possible to provide quantitative data (e.g. in certain histological, histochemical or immunohistochemical investigations) particular care should be taken to indicate how convincing evidence of changes (or lack of change) was obtained.

Abstract Checklist for Authors, Referees, Chairpersons

(Clinical Pharmacology Section)

This checklist is intended to help authors in the preparation of their abstracts, and to assist referees and chairpersons in reviewing abstracts. We hope that it will make it easier for authors to ensure that their abstracts conform with the Society's standards of preparation, and thus allow more time at the meeting for discussion of the scientific content of their work.

One of the authors is a BPS member (or introduced by one) ☐

The hypothesis under investigation and/or the objective of the study are clearly stated ☐

The study has been approved by an ethical committee ☐

The abstract is new with original data ☐

The receptor nomenclature conforms to BJP/TiPS terminology ☐

If this is the first report of a drug with only a serial number, the authors have given the full chemical name ☐

Any non-standard abbreviations are explained ☐

The subjects under study are well described, including numbers ☐

The abstract describes completed work, and no findings are presented which are not in the abstract ☐

The statistical analysis is appropriate ☐

Estimate of variability (SD, s.e.m., range) and precision (95% C.I.s) are given, if appropriate ☐

The abstract contains a conclusion ☐

The conclusion is justified by the results ☐

The references are in the correct format ☐

Do the authors wish the abstract to be published? Yes ☐ No ☐

***In vitro* studies (e.g. drug metabolism)**

The assay details are adequate ☐

Units of measurement are given ☐

It is clear whether numbers given refer to different preparations or replications of the same preparations ☐

Where appropriate, sex, weight and strain of animals are given ☐

British Pharmacological Society

DOSING FOR TWO: PLACENTAL TRANSFER AND FETAL DARUNAVIR EXPOSURE

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Introduction: Fetal drug exposure during pregnancy can be a determinant of fetal drug toxicity or efficacy. Fetal exposure is usually derived from the cord-to-maternal (ctm) concentration ratio. This static parameter does not provide information on the pharmacokinetics *in utero*, limiting the assessment of a fetal exposure-effect relationship. Pregnancy physiologically-based pharmacokinetic (p-PBPK) modelling could provide a solution, although incorporation of placental transfer remains challenging. Here, we aimed to include placental transfer parameters derived from an *ex vivo* human cotyledon perfusion model into a p-PBPK model, to quantitatively simulate fetal exposure to the antiretroviral agent darunavir, co-administered with ritonavir, at term.

Methods: An existing and validated p-PBPK model of maternal darunavir/ritonavir exposure was coded in Berkeley Madonna syntax to allow expansion with a feto-placental unit. Bidirectional placental transport of darunavir at term was included. In order to parameterize the model, we determined maternal-to-fetal (mtf) and fetal-to-maternal (ftm) darunavir/ritonavir placental clearances with an *ex vivo* human cotyledon perfusion model. Simulated maternal PK profiles were compared with observed clinical data to verify the validity of the maternal model aspect. Next, population fetal PK profiles were simulated for different darunavir/ritonavir dosing regimens. These profiles were compared with available cord blood concentrations *in vivo.* Additionally, we explored the influence of different DRV/r dosing regimens on fetal exposure and antiviral effects.

Results: An average (±SD) mtf cotyledon clearance of 0.91±0.11 mL/min and ftm of 1.6±0.3 mL/min was determined (n=6 perfusions). Scaled placental transfer was included into a feto-placental unit and integrated in the p-PBPK model. For darunavir 600/100mg twice daily, the simulated fetal plasma C_{max}, C_{trough}, T_{max} and $T_{1/2}$ at steady state were; 1.1 mg/L, 0.57 mg/L, 3 hours, and 21 hours, respectively. This indicates that the fetal population C_{trough} is above the protein-adjusted EC_{90} for inhibiting the replication of wild type (0.20 mg/L) and around the EC_{90} for resistant virus (0.55 mg/L). The simulated ftm plasma concentration ratio (range) over a dosing interval was 0.30 (0.16 - 0.37), compared to a median (range) ratio for observed darunavir ctm plasma ratio of 0.18 (0 - 0.82; 0 reported if cord blood concentrations were below the lower limit of quantification [<0.09 mg/L] and hence no ratio could be determined).

Conclusion: A p-PBPK model for maternal darunavir exposure was extended with a feto-placental unit. The simulated fetal darunavir plasma concentrations were in the range of observed cord blood concentrations. This advanced model provides a valuable tool in assessing the implications of new dosing regimens, optimizing the safety of maternal pharmacotherapy and fetal antiretroviral treatment.