SCIENTIFIC DISCUSSION

This part reflects the scientific knowledge and the information about this product available at the time of prequalification. Thereafter, updates may have become necessary which are included in parts 1 to 5 and, if related to pharmaceutical issues, also documented in part 8 of this WHOPAR.

Name of the Finished Pharmaceutical Product:	达力嗪 R (DALIQIN)[1]
Manufacturer of Prequalified Product:	Sinopharm Zhijun (Shenzhen) Pharmaceutical Co., Ltd. No. 16, Lanqing Yilu, Hi-Tech Zone Guanlan, Longhua New District Shenzhen China
Active Pharmaceutical Ingredient (API):	Ceftriaxone (as sodium)
Pharmaco-therapeutic group (ATC Codes):	Antibacterials, Third-generation cephalosporins, ATC code: J01DD04. Antimycobacterials, thiocarbamide derivatives (J04AD01)
Therapeutic indication:	达力嗪 R (DALIQIN) is indicated for the treatment of bacterial infections in Human Immunodeficiency Virus (HIV)/AIDS patients.

1 Trade names are not prequalified by WHO. This is the national medicines regulatory authority's responsibility. Throughout this WHOPAR the proprietary name is given as an example only.

1. Introduction

达力嗪 R (DALIQIN) is indicated for the treatment of bacterial infections in Human Immunodeficiency Virus (HIV)/AIDS patients.

达力嗪 R (DALIQIN) should be co-administered with other antibacterial agents whenever the possible range of causative bacteria would not fall within its spectrum.

达力嗪 R (DALIQIN) should be initiated by a health care provider experienced in the management of bacterial infections in Human Immunodeficiency Virus (HIV) /AIDS patients.

2. Assessment of Quality

The assessment was done in accordance with the requirements of WHO's *Guidelines on submission of documentation for a multisource (generic) finished pharmaceutical product for the WHO Prequalification of Medicines Programme: quality part.*

Active pharmaceutical Ingredient (API)
The API is supplied as sterile material. A CEP (Certificate of Suitability) issued by the EDQM was submitted for sterile ceftriaxone sodium, ensuring good manufacturing control and applicability of the Ph.Eur. monograph to control quality of the API.

Other ingredients
The powder for injection contains no excipient.

Finished pharmaceutical product (FPP)

Pharmaceutical development and manufacture
The powder for injection is available as a white or yellowish, crystalline powder in a clear type I glass vial (30ml) closed with a bromobutyl rubber stopper and aluminium cap. Each 30 ml vial contains sterile ceftriaxone sodium equivalent to 1g ceftriaxone.

Similar to the comparator product, Rocephin®, the powder for injection contains no excipient. Sterile ceftriaxone sodium powder, as obtained from the API manufacturer, is filled in to sterile vials, which are stoppered and sealed under aseptic processing.

Specifications
The specifications for the powder for injection include tests for description, identification of API (IR) and sodium, reconstitution time, appearance of solution (clarity and colour), pH, particulate matter (visible and sub-visible particles), related substances (HPLC), water content (KF), bacterial endotoxins, sterility, average mass, uniformity of dosage unit (by mass variation) and assay (HPLC). The analytical methods have been adequately validated.

Stability testing
Stability studies have been performed at 30°C/75%RH (zone IVb) as long-term storage conditions and for six months at accelerated conditions on vials stored in the upright and inverted position. Slight degradation was observed, though the results were within justified limits. No potential extractables were detected. Based on the available stability data, the proposed shelf life and storage conditions of the unopened vials as stated in the SmPC are acceptable.

The in-use storage times and conditions of the solutions for injection and infusion appearing in the SmPC are supported by in-use chemical and physical stability testing.

Conclusion
The quality part of the dossier is accepted.

3. Assessment of Bioequivalence

The applicant requests a biowaiver as per WHO Technical Report Series, No. 992 which indicates that no bioequivalence study is necessary when the pharmaceutical product is to be administered parenterally (e.g. intravenously, subcutaneously or intramuscularly) as an aqueous solution containing the same API in the same molar concentration as the comparator product and the same or similar excipients in comparable concentrations as in the comparator product.
The appropriate comparator product is Rocephin (ceftriaxone, 1 g powder for solution for injection, Roche). Rocephin contains 1 g ceftriaxone with no excipients. The composition of the proposed product is the same i.e., it contains only 1 g ceftriaxone.

As the proposed product meets the biowaiver requirements described above, a biowaiver can be granted.

4. Summary of Product Safety and Efficacy

达力嗪 R (DALIQIN) has been shown to conform to the same relevant standards of quality, efficacy and safety as those required of the innovator product. According to the submitted data on quality 达力嗪 R (DALIQIN) is pharmaceutically and therapeutically equivalent and thus interchangeable with the innovator product Rocephin® 1 g powder for injection Rocephin for which benefits have been proven in terms of clinical efficacy.

The clinical safety of this product is considered to be acceptable when guidance and restrictions as stated in the Summary of Product Characteristics are taken into account. Reference is made to the SmPC (WHOPAR part 4) for data on clinical safety.

5. Benefit risk assessment and overall conclusion

Quality

Physicochemical and biological aspects relevant to the uniform pharmaceutical characteristics have been investigated and are controlled in a satisfactory way. The quality of this product is considered to lead to an acceptable clinical performance when 达力嗪 R (DALIQIN) is used in accordance with the SmPC.

Bioequivalence
N/A

Efficacy and Safety

Regarding clinical efficacy and safety, 达力嗪 R (DALIQIN) is considered effective and safe to use when the guidance and restrictions in the Summary of Product Characteristics are taken into consideration.

Benefit Risk Assessment

Based on WHO's assessment of data on quality, bioequivalence, safety and efficacy the team of assessors considered that the benefit–risk profile of 达力嗪 R (DALIQIN) was acceptable for the following indication:**"treatment of bacterial infections in Human Immunodeficiency Virus (HIV)/AIDS patients"** and has advised that the quality, efficacy and safety of 达力嗪 R (DALIQIN) allow inclusion of 达力嗪 R (DALIQIN), manufactured at Sinopharm Zhijun (Shenzhen) Pharmaceutical Co., Ltd., No. 16, Lanqing Yilu, Hi-Tech Zone, Guanlan, Longhua New District, Shenzhen, China, in the list of prequalified medicinal products.