 

**ISARIC/WHO Severe Acute Respiratory Infection Biological Sampling Study**

**SUMMARY**

**13th May 2013. Version 2.5.1**

**Setting up research studies.**

The World Health Organisation supports the conduct of investigator-led clinical research in outbreaks of emerging infection. In order to facilitate this, the following two options are recommended for the use of this research protocol:

1. Use these documents independently of, and with no obligations to, WHO. Studies using this protocol will be compatible with other studies around the world, enabling future collaboration on data analysis as needed.
2. Use these documents in collaboration with WHO and ISARIC to ensure rapid set up and analysis. ISARIC can help to link investigators to laboratories currently working on relevant analyses, and access to a secure online database for clincal data collection; WHO can provide additional resources in low- and middle-income countries to enable data and sample collection.

Tiers included in this protocol are:

Tier 1 (Single biological sample) - Clinical samples will be collected on enrolment day (Day 1; ideally at initial presentation to a health care facility). Clinical information will be collected at enrolment and discharge.

Tier 2 (Serial biological sampling) - Clinical samples and data will be collected on enrolment day (Day 1; ideally at initial presentation to a health care facility), and then alternate days for the first 2 weeks, then weekly until resolution of illness or discharge from hospital, and again at 3 and 6 months after enrollment.

Tier 3C (Population pharmacokinetics of antimicrobial/immunomodulatory drugs)

Table 2. Sampling pattern - In Patient Recruitment

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Serial samples. | | | | | | | | | | | | | | |  |
|  | Recruitment | Week 1 | | | | | | Week 2 | | | | | | |  | Further samples | Convalescent samples |
| Day | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | Weekly until max 100 days | 3 months and 6 months after recruitment |
| >40kg | R |  | S |  | S |  | S |  | S |  | S |  |  |  |  | S | C |
| 20 to 40kg | R |  | S |  | S |  | S |  | S |  | S |  |  |  |  | S | C |
| 10 to 20kg | R |  | S |  | S |  | S |  | S |  | S |  |  |  |  | S | C |
| 4 to 10kg | R |  | S |  | S |  | P |  | S |  | P |  |  |  |  | S | C |
| >4kg | R |  | S |  | S |  | P |  | S |  | P |  |  |  |  | S | C |
| Sample priority | 1 |  | 2 |  | 5 |  | 7 |  | 3 |  | 8 |  |  |  |  | 6 | 4 |

R = recruitment samples. S = serial samples including pathogen samples; P = research pathogen samples only; C = convalescent samples (see Table 3). In the event that local resource limitations require sampling frequency to decrease, samples will be prioritised as shown (1=highest priority).

Table 3. Samples

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Weight | Samples at recruitment (R) | Serial samples (S) | Convalescent samples | Total Volumes of blood taken |
| >40kg | 9mls EDTA blood  3mls blood in serum(clotted) tube  3mls blood in blood RNA tube  Research pathogen samples | 3mls EDTA blood  3mls blood in serum(clotted) tube  3mls blood in blood RNA tube  Up to 3 additional 1ml samples in EDTA or fluoride oxalate tubes spread throughout dosing schedule for pharmacokinetic/pharmacodynamic studies.  Research pathogen samples | 3mls EDTA blood  3mls blood in serum(clotted) tube  3mls blood in blood RNA tube  Research pathogen samples | Maximum any day: 15mls (0.38mls/kg)  Maximum any 4 weeks: 96mls (maximum 2.4mls/kg) |
| 20 to 40kg | 6mls EDTA blood  3mls blood in serum(clotted) tube  3mls blood in blood RNA tube  Research pathogen samples | 1mls EDTA blood  2mls blood in blood RNA tube  Up to 3 additional 0.5ml samples in EDTA or fluoride oxalate tubes spread throughout dosing schedule for pharmacokinetic/pharmacodynamic studies.  Research pathogen samples | 1mls EDTA blood  3mls blood in serum(clotted) tube  2mls blood in blood RNA tube  Research pathogen samples | Maximum any day: 12mls (0.6mls/kg)  Maximum any 4 weeks: 42mls (maximum 2.1mls/kg) |
| 10 to 20kg | 2mls EDTA blood  2mls blood in serum(clotted) tube  2mls blood in blood RNA tube  Research pathogen samples | 1mls EDTA blood  1mls blood in blood RNA tube  Up to 3 additional 0.2ml samples in EDTA or fluoride oxalate tubes spread throughout dosing schedule for pharmacokinetic/pharmacodynamic studies.  Research pathogen samples | 1mls EDTA blood  1mls blood in serum(clotted) tube  1mls blood in blood RNA tube  Research pathogen samples | Maximum any day: 6mls (0.6mls/kg)  Maximum any 4 weeks: 23.6mls (maximum 2.36mls/kg) |
| <4 to 10kg | 1mls EDTA blood  1mls blood in serum(clotted) tube  mls blood in blood RNA tube  Research pathogen samples | 1mls EDTA blood  Up to 3 additional 0.2ml samples in EDTA or fluoride oxalate tubes spread throughout dosing schedule for pharmacokinetic/pharmacodynamic studies.  Research pathogen samples | 1mls EDTA blood  1mls blood in serum(clotted) tube  Research pathogen samples | Maximum any day: 2mls (0.5mls/kg)  Maximum any 4 weeks: 9.4mls (maximum 2.35mls/kg) |
| < 4kg | 0.5mls EDTA blood  0.1mls blood in serum(clotted) tube  mls blood in blood RNA tube  Research pathogen samples | 0.2mls EDTA blood  Up to 3 additional 0.1ml samples in EDTA or fluoride oxalate tubes spread throughout dosing schedule for pharmacokinetic/pharmacodynamic studies.  Research pathogen samples | 0.2mls EDTA blood  0.2mls blood in serum(clotted) tube  Research pathogen samples | Maximum any day: 0.8mls (~0.27mls/kg)  Maximum any 4 weeks: 2.4mls (maximum 2.4mls/kg) |
| Research pathogen samples (all patients) | Pathogen samples taken solely for research purposes:   1. In all patients: combined nose and throat swab 2. In all intubated patients: endotracheal aspirate   also where resources permit:   1. Nasopharyngeal aspirate (NPA) OR (if NPA impossible) flocked nose and throat swab 2. Urine (up to 10mls in sterile universal container, if available) 3. Rectal swab or stool (up to 10mls in sterile universal container or stool specimen container, if available) 4. samples/swabs from infected sites or sores. | | | No patient will give more than 0.6mls/kg (>1% blood volume) on any one day, or more than 2.4mls/kg (approx 3% blood volume) in any four week period (MCRN recommendations). |
| Clinician-requested pathogen samples (all patients) | Where possible, we will obtain an aliquot of any residual and unwanted sample volume from specimens that have been sent by clinicians for pathogen detection, including those obtained before recruitment to the study: urine; stool; respiratory tract samples (NPA, ETA, BAL, sputum, ENT swabs); cerebrospinal fluid. | | |  |