


<b>GA 101003666</b> <b>Start Date: 01/04/20</b> <b>End Date: 31/03/22</b>	
<b>Project Title</b>	OPENCORONA
<b>WP number, deliverable number, and Title</b>	WP 5 D5.1 Pre-Production Evaluation and plasmid production for toxicology studies
<b>Responsible partner name and contact</b>	Partner number: 5 Organisation: Cobra Biologics Name: Ola Tu vesson Email: Ola.Tu vesson@cobrabio.com
<b>Nature</b> R-Report P-Prototype D-Demonstrator O=-Other	Report
<b>Dissemination level</b> <b>PU</b> -public <b>PP</b> -restricted to other programme participants <b>RE</b> -restricted to a group of partners <b>CO</b> -only for consortium members	Public
<b>Delivery Month Planned</b>	10 (31/1/21)
<b>Actual delivery date (dd/mm/yy)</b>	31/3/21



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# Description of deliverable

## • COMPLETED

### **D5.1 Pre-Production Evaluation and plasmid production for toxicology studies**

To evaluate the processability of the plasmid and to manufacture plasmid bulk drug substance to be used for toxicology studies Cobra Biologics set up and manufactured a down scale non GMP batch, e.g., HQ DNA Batch. The work executed includes generation of a Production Cell Bank (PCB) with the intended plasmid, a fermentation run in 15L scale and subsequent downstream processing in order to isolate and purify the expressed plasmid. The HQ DNA batch (HQD2003) was manufactured from 2020-10-12 to 2020-11-30 at Cobra Biologics with the plasmid OC2.3 provided by Karolinska Institutet. A total of 250 vials were filled with 1 mL of purified DNA at 2.0 mg/mL. The batch documentation was reviewed after manufacturing and a CoT and BSE/TSE certificate were emitted. Adlego requested 35 vials to perform toxicology studies. On the 16th of December, Adlego received all the requested HQ material. Apart from this, 10 vials of HQ material were also delivered to KI for the use in immunological and toxicological studies in macaques and rabbits.

The pre-production evaluation in HQ manufacturing scale confirms that the cells grow and express plasmid to the expected levels and there is no reason not to progress to larger scale engineering runs to further confirm the process in large scale.

A total of 24 vials of purified DNA were submitted to the planned stability study to gain initial stability data to support the storage of the first GMP material. The samples were submitted to an accelerated stability study for 6 months at  $25^{\circ}\text{C} \pm 2^{\circ}\text{C}/60\% \text{ RH} \pm 5\% \text{ RH}$  and long-term stability at  $5^{\circ}\text{C} \pm 3^{\circ}\text{C}/\text{amb.}$  for 12 months.

The test results for the accelerated study at 1 month and 2 months showed an unexpected high degradation in the supercoiled form of the DNA. However, the initial design of the stability study did not represent the adequate condition to store a DNA vaccine. Since the intended temperature for storage of the plasmid will be  $-20^{\circ}\text{C}$  a new stability study was started to better understand the periodic degradation and demands in which the DNA keeps its form after manufacturing. The actual accelerated study was discontinued since the ICH guide (ICH Topic Q 1 A (R2)) states that if a significant change occurs within the first 3 months' testing at the accelerated storage condition, it is considered unnecessary to continue to test a drug substance through 6 months. A new long-term stability study was initiated 2021-02-16 at  $-20^{\circ}\text{C} \pm 5^{\circ}\text{C}$  for 12 months. The data to be obtained under this temperature will provide initial evidence for the storage and expiration date for the GMP DNA material. Subsequently also the GMP material will be put on stability.

## • STILL ONGOING

### **D5.1 Pre-Production Evaluation and plasmid production for toxicology studies**

The accelerated and long-term stability study is ongoing. The results will be summarized in an internal report after 6 months and 12 months, respectively.

## • PUBLICATIONS

Not applicable for Cobra work package.

