RINGKASAN HASIL EVALUASI
PERMOHONAN PERSETUJUAN PELAKSANAAN UJI KLINIK
VAKSIN HEPATITIS B *BRIDGING STUDY*
PRODUKSI PT. BIOFARMA

Informasi Umum

1. Hepatitis B dengan bahan aktif HBsAg impor dari *The Jannsen Vaccine Corp* telah terdaftar di Indonesia dengan produsen dan pendaftar PT. Bio Farma, Tbk. (GKL9802905543A1). Uji klinik diajukan dikarenakan perubahan vendor bulk Vaksin Hepatitis B (Inactive HbsAg) menjadi Serum Institute of India (SII).
2. Pendaftar berencana akan mendapatkan suplai bulk Hepatitis B dari SII yang telah terdaftar di negaranya dan telah prekualifikasi WHO sambil menunggu vaksin Hepatitis B produksi Bio Farma siap dipasarkan yang saat ini masih dalam tahap Obat Pengembangan Baru (OPB).

Informasi Uji Klinik

1.	Judul Protokol	:	***Protectivity and Safety Following Recombinant Hepatitis B Vaccine with different source of Hepatitis B bulk compared to Hepatitis B (Bio Farma) vaccine in Indonesian Population*** (versi 1.a, Maret 2019)
2.	Produk Uji	:	Recombinant Hepatitis B (*bulk SII*) (HbsAg 20 mcg) diberikan 3 kali secara intramuskular Produsen PT. Bio Farma
3.	Produk Pembanding	:	Recombinant Hepatitis B (*registered vaccine (Bulk Janssen)*) (HbsAg 20 mcg) diberikan 3 kali secara intramuskular Produsen PT. Bio Farma
4.	Center / Peneliti	:	Fakultas Kedokteran Universitas Diponegoro / Dr. Yetty Movieta Nency, SpA(K)
5.	Sponsor / ORK	:	PT. Bio Farma
6.	Persetujuan Etik	:	No. 80/EC/FK UNDIP/III/2019 tanggal 22 Maret 2019 dari Komisi Etik Penelitian Kesehatan Fakultas Kedokteran Universitas Diponegoro
7.	Desain Uji Klinik	:	*Experimental, randomized, double blind, four arm parallel group study*
8.	Jumlah Subjek	:	*536 subjects (10-40 years old)*
9.	Tujuan Uji Klinik	:	*Primary Objective* *To asses the protectivity of investigational product after three doses of vaccine in children, adolescents and adults.* *Secondary Objective* - *To describe immunogenicity of investigational product in all subjects.* - *To assess the safety of investigational product in all subjects.* - *To evaluate immunogenicity and safety after primary series of investigational product compare to control* - *To evaluate immunogenicity and safety in three consecutive batches of investigational product in all subjects*
10.	Kriteria Eligibilitas	:	Kriteria Inklusi / *Inclusion criteria* *1. Healthy individu as determined by clinical judgment, including a medical history and physical exam which confirms the absence of a*

current or past disease state considered significant by the investigator.

2. *Subjects/parents/guardian(s) have been informed properly regarding the study and signed the informed consent form/informed assent form.*
3. *Subject/parents/guardian(s) will commit to comply with the instructions of the investigator and the schedule of the trial.*

Kriteria Eksklusi / *Exclusion criteria*

1. *Subject concomitantly enrolled or scheduled to be enrolled in another trial.*
2. *Subjects with known history of Hepatitis B contained vaccination in the last 10 years*
3. *Evolving severe illness and/or chronic disease and fever (axillary temperature ≥37.5^{0}C) within the 48 hours preceding enrollment.*
4. *Known history of allergy to any component of the vaccines (based on anamnesis)*
5. *HBsAg positive*
6. *Known history of immunodeficiency disorder (HIV infection, leukemia, lymphoma, or malignancy).*
7. *History of uncontrolled coagulopathy or blood disorders contraindicating intramuscular injection.*
8. *Subject who has received in the previous 4 weeks a treatment likely to alter the immune response (intravenous immunoglobulins, blood-derived products or corticosteroid therapy and other immunosuppresant.*
9. *Pregnancy & Lactation (Adult)*
10. *Subject already immunized with any vaccine within 4 weeks prior and expects to receive other vaccines within 4 weeks following immunization.*

11. Luaran Uji Klinik/*Endpoint* **:**

Luaran Primer */ Primary Endpoints*:
number and percentage of subjects with anti HbsAg > 10mIU/ml, 28 days after the primary series of Hepatitis B vaccination for each group.

Luaran Sekunder */ Secondary endpoints*

Immunogenicity

- *Serological response to the Hepatitis B vaccine recombinant : Geometric mean of anti-HbsAg, percentage of subjects with increasing antibody titer ≥ 4 times and/ or percentage of subjects with transition of seronegative to seropositive*
- *Comparison of GMT, seroprotection, percentage of subjects with increasing antibody titer ≥ 4 times and/ or percentage of subjects with transition of seronegative to seropositive following primary series of investigational product compare to control.*
- *Comparison of GMT, seroprotection, percentage of subjects with increasing antibody titer ≥ 4 times and/ or percentage of subjects*

with transition of seronegative to seropositive following primary series between each number of investigational product.

Safety

- *Immediate reaction within the first 30 minutes after each injection.*
- *Local and systemic events occurring within 72 h after each injection*
- *Local and systemic events occurring between 72h and 28 days following injection.*
- *Any serious adverse event occurring from inclusion until 28 days after the last injection*
- *Comparison of adverse events between investigational product (IP) and control.*
- *Comparison of adverse events between each batch number of IP*

Ringkasan Hasil Evaluasi

Badan POM telah melakukan evaluasi protokol yang diajukan yang didukung oleh tim ahli melalui rapat pada tanggal 1 Juli 2019 dengan hasil sebagai berikut:

1. Uji klinik dilakukan karena adanya perubahan *vendor* bulk Vaksin Hepatitis B (Inactive HbsAg) yang semula berasal dari *The Janssen Vaccine Corp* menjadi *Serum Institute of India (SII)*. Uji klinik dilakukan untuk membandingkan imunogenisitas dan keamanan kedua vaksin.
2. Desain uji klinik yang diajukan dapat diterima. Vaksin Hepatitis B yang disetujui dapat diberikan untuk semua kelompok usia namun uji klinik ini hanya akan mengikutsertakan subjek usia 10 – 40 tahun, sedangkan untuk usia kecil 10 tahun akan dilakukan pada studi terpisah Pentabio.
3. Vaksin memenuhi persyaratan mutu.

Keputusan

Pelaksanaan uji klinik dengan protokol di atas disetujui melalui penerbitan Persetujuan Pelaksanaan Uji Klinik (PPUK) No. B-PN.01.06.3.32.321.07.19.2543 tanggal 18 Juli 2019.