**RINGKASAN HASIL EVALUASI**
**PERMOHONAN PERSETUJUAN PELAKSANAAN UJI KLINIK**
**VAKSIN HEPATITIS B FASE I**
**PRODUKSI PT. BIO FARMA**

**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). Untuk memenuhi suplai vaksin program imunisasi nasional dan kemandirian ketersediaan vaksin, PT. Bio Farma mengembangkan bulk hepatitis B yang diproduksi sendiri (*in-house production*) dan mengajukan uji klinik melalui jalur penilaian Obat Pengembangan Baru (OPB).
2. Pengajuan uji klinik fase 1 Vaksin Hepatitis B didukung oleh uji nonklinik berupa uji toksisitas akut dan kronik pada hewan tikus dan kelinci.

**Informasi Uji Klinik**

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| 1. | Judul Protokol | : | ***Safety and Preliminary of Immunogenicity Following Recombinant Hepatitis B (Bio Farma) Vaccine in Adults & Children*** (versi 2.0, Juli 2019) |
| 2. | Produk Uji | : | Recombinant Hepatitis B (*inhouse vaccine*) (HbsAg 20 mcg) diberikan 1 kali (untuk anti-HBs ≥ 10 mIU/ml) dan 3 kali (untuk anti-HBs < 10 mIU/ml) secara intramuskular<br>Produsen PT. Bio Farma |
| 3. | Produk Pembanding | : | Recombinant Hepatitis B (*registered vaccine*) (HbsAg 20 mcg) diberikan 1 kali (untuk anti-HBs ≥ 10 mIU/ml) dan 3 kali (untuk anti-HBs < 10 mIU/ml) secara intramuskular<br>Produsen PT. Bio Farma |
| 4. | Center / Peneliti | : | Prof. Dr. Kusnandi Rusmil, dr., Sp.A(K)., MM / RSUP Dr. Hasan Sadikin, Bandung / Fakultas Kedokteran, Universitas Padjadjaran, Bandung<br>*Fieldsite:* Puskesmas Garuda |
| 5. | Sponsor / ORK | : | PT. Bio Farma |
| 6. | Persetujuan Etik | : | No. 1030/UN6.KEP/EC/2019 tanggal 5 Agustus 2019 dari Komisi Etik Penelitian Universitas Padjadjaran, Bandung |
| 7. | Desain Uji Klinik | : | *Experimental, randomized, double blinded, prospective intervention study* |
| 8. | Jumlah Subjek | : | *100 healthy subjects (10-40 years old)* |
| 9. | Tujuan Uji Klinik | : | ***Primary Objective***<br>*To assess immediate reaction within the first 30 minutes after one dose or three doses of Hepatitis B vaccination depends on anti-HBs titer before immunization.*<br><br>***Secondary Objective***<br>- *To describe the safety following one dose or three doses of Hepatitis B vaccination depends on anti-HBs titer before immunization*<br>- *To assess preliminary information of immunogenicity following one dose or three doses of Hepatitis B vaccination depends on anti-HBs titer before immunization*<br>- *To compare the safety and preliminary information on immunogenicity of the trial vaccine with the control registered vaccine* |



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10. Kriteria Eligibilitas : ***Inclusion criteria***

*Adult:*

1. *Healthy individu as determined by clinical judgment, including a medical history, physical exam, rontgen thorax and laboratory results, which confirms the absence of a current or past disease state considered significant by the investigator.*
2. *Subjects have been informed properly regarding the study and signed the informed consent form*
3. *Subjects will commit to comply with the instructions of the investigator and the schedule of the trial.*

*Children:*

1. *Healthy individu as determined by clinical judgment, including a medical history, physical exam and rontgen thorax 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 and*
3. *Subject/parents/guardian(s) will commit to comply with the instructions of the investigator and the schedule of the trial.*

***Exclusion criteria***

1. *Subject concomitantly enrolled or scheduled to be enrolled in another trial*
2. *Any direct relatives relationship with the study team.*
3. *Evolving mild, moderate or severe illness, especially infectious diseases or fever (axillary temperature ≥ 37.5°C) within the 48 hours preceding enrollment.*
4. *Known history of allergy to any component of the vaccines (based on anamnesis)*
5. *Known history of immunodeficiency disorder (HIV infection, leukemia, lymphoma, or malignancy)*
6. *History of uncontrolled coagulopathy or blood disorders contraindicating for phlebotomy.*
7. *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).*
8. *Any abnormality or chronic disease which according to the investigator might interfere with the assessment of the trial objectives.*
9. *Pregnancy or planning a pregnancy within the next 3 months & lactation. (for Adults)*
10. *Subject already immunized with any vaccine within 4 weeks prior and expects to receive other vaccines within 4 weeks following immunization.*
11. *HbsAg positive*
12. *Subjects with known history of Hepatitis B infection.*



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13. *Subjects who have received Hepatitis B vaccination which proven by vaccination records.*
14. *Subject planning to move from the study area before the end of study period.*

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

*Number and percentage of subjects with at least one immediate reaction (local reaction or systemic event) within 30 minutes after one dose or three doses of Hepatitis B vaccination.*

***Secondary endpoints***

*Safety*

- *Number and percentage of subjects with at least one of these adverse events, solicited or not, within 24 h, 48h, 72h and 28 days after each dose of vaccination.*
- *Number and percentage of subjects with serious adverse event from inclusion until 28 day after each dose of vaccination.*
- *Any deviation from routine laboratory evaluation that probably related to the vaccination (adults subject)*
- *Description of safety data between groups*

*Immunogenicity:*

*Preliminary assessment of immunogenicity of anti-HBs following 1 dose of vaccination*

- *Number and percentage of subjects with anti HbsAg ≥10mIU/ml, 28 days after 1 doses of vaccination*
- *Number and percentage of subjects with ≥ 4 times increasing antibody*
- *Geometric Mean Titers (GMT) following immunization*
- *Anti-HBs description between groups*

*For subjects with anti-HBs not protective (<10 mIU/ml) before immunization:*

*Immunogenicity: Preliminary assessment of immunogenicity of anti-HBs following 3 doses of vaccination:*

- *Number and percentage of subjects with anti HbsAg ≥ 10mIU/ml, 28 days after 3 doses of vaccination.*
- *Number and percentage of subjects with ≥ 4 times increasing antibody*
- *Geometric Mean Titers (GMT) following immunization*

**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. Berdasarkan hasil studi toksisitas akut, kronis dan satelit pada hewan tikus dan kelinci menggunakan 3 bets vaksin Hepatitis B menunjukkan vaksin aman, vaksin tidak mempengaruhi pertumbuhan dan berat badan, konsumsi pakan, suhu tubuh, perubahan perilaku, komposisi urin, gambaran hematologi, gambaran biokimia darah, kondisi umum organ, tidak ada efek toleran lokal, dan tidak menyebabkan perubahan gambaran sel dalam uji histopatologi.
2. Desain uji klinik fase 1 yang diajukan dapat diterima.
3. Vaksin memenuhi persyaratan mutu.

**Keputusan**

Pelaksanaan uji klinik dengan protokol di atas disetujui melalui penerbitan Persetujuan Pelaksanaan Uji Klinik (PPUK) No. RG.01.06.321.11.19.4608 tanggal 18 November 2019.



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