REFERENCE SUBSTANCES

PERTEMUAN ILMIAH TAHUNAN IAI, JAKARTA, 6 SEPT 2017

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Pusat Pengujian Obat dan Makanan Nasional, BPOM

OUTLINE

- DEFINITION
- Assesment of need for the establishment RS in pharmaceutical
- Establishment Process of Reference Substance
- Establishment of BPFI Production in Indonesia
- Challenges of BPFI Production in Indonesia

DEFINITION

- Reference substance is an authenticated, uniform material that is intended for use in specified chemical and physical tests, in which its properties are compared with those of the product under examination, and which possesses a degree of purity adequate for its intended use.

- Pharmacopoeial reference standards are Pharmacopoeial standards and substances are established and distributed by pharmacopoeial authorities following the general principles of this Guide. It should be noted, however, that a different approach is used by the pharmacopoeial authorities to give the user the information provided by certificate of analysis and expiration dates.

Definition

Primary RS

- Widely acknowledged to have the appropriate qualities within a specified context.
- Whose assigned content when used as an assay standard is accepted without requiring comparison with another chemical substances

Secondary RS

- Whose characteristics are assigned and/or calibrated by comparison with a primary RS.
- The testing of secondary RS may be less than for a primary RS
- Ussually intended and supplied as official, e.g regional/national standards.

Working standards refers to secondary RS establish by manufacturer or laboratories

Definition

- Baku Pembanding Farmakope Indonesia (BPFI)
  - Adalah senyawa yang telah disetujui keabsahan penggunaannya sebagai pembanding dalam pengujian dan penetapan kadar berdasarkan Farmakope Indonesia.
  - Dibuat dan diedarkan dibawah wewenang Badan Pengawas Obat dan Makanan.

Definition

- International Chemical Reference Substances
  - Are primary chemical reference substances for use in physical and chemical tests and assays described in The International Pharmacopoeia or in other WHO quality assurance documents adopted by the WHO Expert Committee on Specification for Pharmaceutical Preparations.
  - ICRS are established and released under the authority of the WHO Expert Committee on Specifications for Pharmaceutical Preparations.

Definition

- British Pharmacopoeia Chemical Reference Substances (BPCRS)
  - BPCRS are established and released under the authority of the British Pharmacopoia Commission
- United States Pharmacopeia Reference Substances (USPRS)
  - Is an authentic specimens that have been approved as suitable for use as comparison standards in US or NF tests and assay

Assesment of need for the establishment RS in pharmaceutical

- To achieve accuracy and reproducibility of the analytical results required by pharmacopoeial testing and pharmaceutical control. (Verifiying the performance of the test methods)
- Considered as an integral part of compliance-oriented monograph or test procedure used to demonstrate the identity, purity and content of pharmaceutical substances and preparations.
- assess system suitability during analyses and to calibrate analytical instruments.

Source Material

- Source material can be selected from a batch (lot) of the substance originating from the normal production process, if the purity is acceptable. The purity requirements for a chemical reference substance depend upon its intended use.
- A purity of 99.5% or higher is desirable, calculated on the basis of the material in its anhydrous form or free of volatile substances. However, the most important consideration is the influence of the impurity on the attribute measured in the assay when used in a nonspecific assay procedure.

Source Material

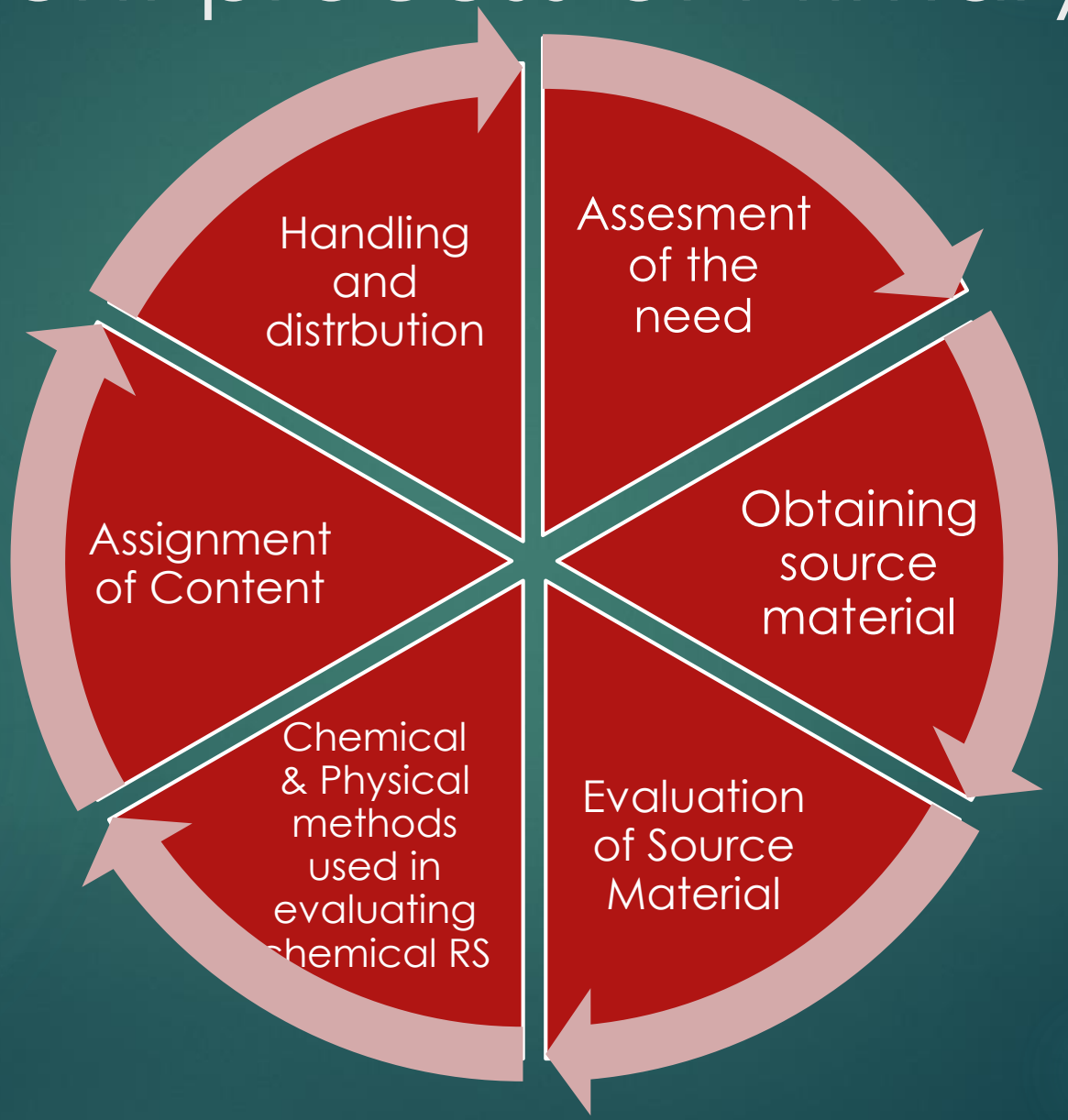
- When source material is obtained from a supplier, the following should be supplied with the material:
  - certificate of analysis (test methods, values found and number of replicates, spectra and/or chromatograms);
  - results of any accelerated stability studies;
  - information on optimal storage conditions required to ensure stability (temperature and humidity considerations);
  - results of any hygroscopicity study and/or statement of the hygroscopicity of the source material;
  - identification of impurities detected;
  - updated material safety data sheet

Analytical procedures used in specifications for pharmaceutical

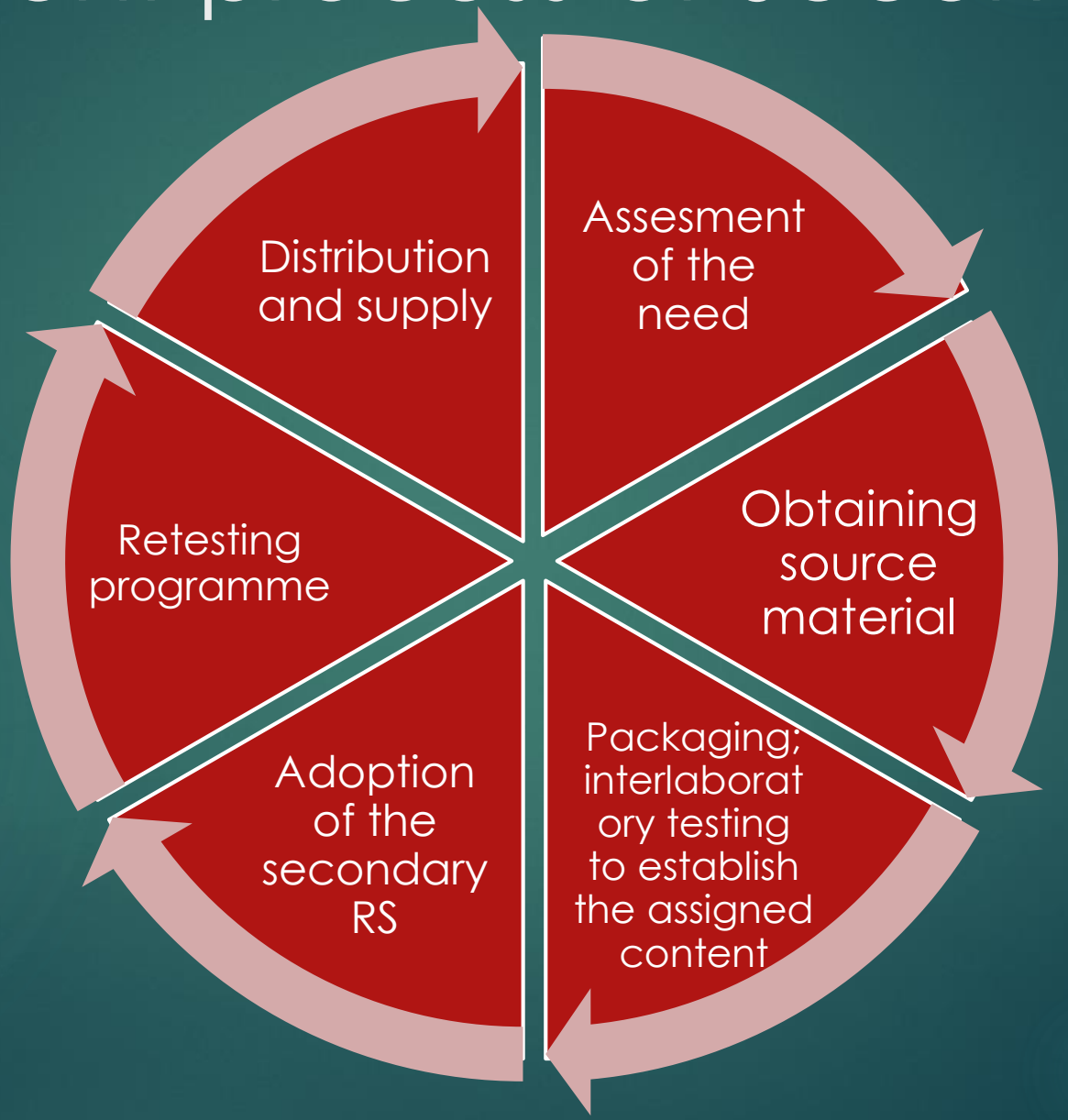
- Infrared (IR) spectrophotometry
- Ultraviolet (UV) absorption spectrophotometry
- Chromatographic separation
- Titrimetric
- Gravimetrics
- Optical rotation

Etc.

Establishment process of Primary RS

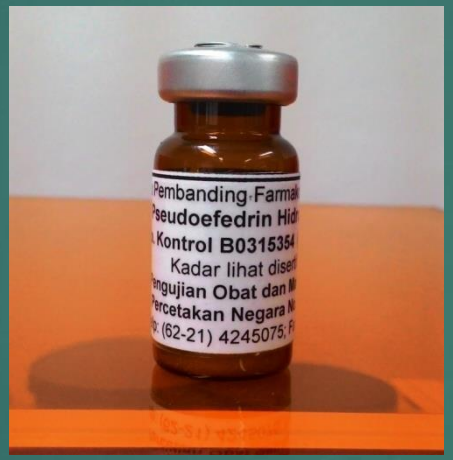


Establishment process of Secondary RS



Establishment of RS in Indonesia

- Baku pembanding Farmakope Indonesia (BPFI) as the primary RS for the intended use In Farmakope Indonesia.
- BPFI is establish and distribute in the authority of Badan POM in Indonesia



Encourages awareness from the manufacturers as the source material in a qualified purity degree

PPOMN sebagai laboratorium Pengembangan Baku Pembanding

- Pengadaan Bahan Baku Pembanding dan Baku Primer
- Pengujian Calon Baku Pembanding
- Uji Kolaborasi Baku Pembanding
- Rapat Adopsi Baku Pembanding dengan Tim Ahli
- Penerbitan Sertifikat Baku Pembanding
- Distribusi Baku Pembanding
- Uji Ulang dalam rangka Stabilitas

Tantangan dan Permasalahan

- **Pengadaan Bahan Baku Pembanding dan Baku Primer**
- → Bahan Baku umumnya diperjualbelikan dalam kuantitas besar sebagai bahan baku Obat untuk Industri.
- → Dalam Pembuatan Baku Pembanding Sekunder maupun BPFI diperlukan bahan baku dalam jumlah sedikit, tidak banyak Supplier yang bersedia mengadakan bahan baku tsb
- → Supplier bahan baku dari luar negeri (impor) agak sulit dalam proses pengadaan. Biaya cukai dan pengiriman belum dapat diperkirakan dalam penganggaran, sehingga kesulitan dalam penetapan harga perkiraan sendiri (HPS)
- **Uji Kolaborasi Baku Pembanding**
- → Masih perlu kolaboran Uji Baku Pembanding yang lebih dapat menjamin validitas hasil Uji
- **Rapat Adopsi Baku Pembanding dengan Tim Ahli**
- → Anggota Tim Adopsi harus mewakili dari berbagai instansi terkait (akademisi, industri, laboratorium kolaboran dll)

Tantangan dan Permasalahan

- Challenges in BPFI establishment :
- Perlu pemahaman bagi Industri untuk mendukung penggunaan BPFI
- Dukungan Industri Untuk penyediaan bahan baku dengan kualitas dan kemurnian yang memadai
- Kolaborasi dengan beberapa sector terkait (Industri, Akademisi, Laboratorium Uji dll) dalam pengujian Baku Pembanding untuk mendapatkan hasil yang lebih baik.

KEPUTUSAN KEPALA BADAN PENGAWAS OBAT DAN MAKANAN REPUBLIK INDONESIA NOMOR : HK.00.05.3.1950 TENTANG KRITERIA DAN TATA LAKSANA REGISTRASI OBAT

Bagian Ketiga

Registrasi

- Pasal 17 (1) Untuk keperluan evaluasi mutu, pendaftar harus menyerahkan contoh obat untuk 3 (tiga) kali pengujian dan bahan baku pembanding sesuai spesifikasi dan metoda pengujian zat aktif dan obat dimaksud. (2) Dikecualikan dari ketentuan sebagaimana dimaksud pada ayat (1) untuk obat copy, penyerahan contoh obat dan bahan baku pembanding adalah apabila diperlukan. (3) Pelaksanaan penyerahan contoh obat dan bahan baku pembanding sebagaimana dimaksud pada ayat (1) dan ayat (2) akan ditetapkan tersendiri oleh Kepala Badan.

TERIMA KASIH