独立行政法人医薬品医療機器総合機構

令和元年度アジア諸国
医薬品・医療機器規制
情報収集・分析事業

調査報告書

令和 2 年 3 月
（2020 年）

GMC 株式会社

令和 元年度アジア諸国医薬品・医療機器規制情報収集・分析事業
調査報告書

目次

参考資料

NATIONAL MEDICINES REGULATORY AUTHORITY ACT, No. 5 OF 2015
GUIDELINE ON REGISTRATION OF MEDICINES
GUIDELINE FOR REGISTRATION OF MEDICAL DEVICES IN SRI LANKA

第１章 調査概要

1.1 調査の目的

アジア諸国において、日本の医薬品・医療機器規制（以下「規制」という。）の理解を促すため、平成28 年4 月に、規制に関するアジア諸国の規制当局の人材の育成機関「アジア医薬品・医療機器トレーニングセンター」（以下「センター」という。）を独立行政法人医薬品医療機器総合機構（以下「機構」という。）に設置し、国内及び海外で研修等を実施している。

より効果的な研修等の企画・立案及び実施に当たっては、研修等の対象となる国・地域での最新の医薬品・医療機器規制に関する情報を収集・分析しておく必要がある。

このため、今後センターによる研修等が予定されている国の各々について、研修等の企画・立案及び実施に当たって基本的な情報となる最新の医薬品及び医療機器に関する規制情報の収集及び分析業務を実施するものである。

1.2 調査対象国の概況

本調査の対象国は、スリランカ民主社会主義共和国（以下、「スリランカ」とする。）である。スリランカの一般概況を以下に記述する。

スリランカの一般概況

スリランカは、南アジアのインド亜大陸の南東にポーク海峡を隔てて位置する共和制国家。首都はスリジャヤワルダナプラコッテ。

1948 年 2 月 4 日、イギリスから自治領（英連邦王国）のセイロンとして独立。1972 年にはスリランカ共和国に改称し、英連邦内の共和国となり、1978 年から現在の国名となった。人口は約 2,167 万人（2018 年）である。島国で、現在もこの国が占める主たる島をセイロン島と呼ぶ。国名をスリランカに改称したシリマヴォ・バンダラナイケは世界初の女性首相である。また、国民の 7 割が仏教徒（上座部仏教）である。

国の花は青睡蓮、国の石はブルーサファイア、国技はバレーボール。

表 1-1：スリランカの一般概況

国・地域名	スリランカ民主社会主義共和国 Democratic Socialist Republic of Sri Lanka
面積	6 万 5,610 平方キロメートル（日本の 0.17 倍）
人口	2,167 万人（2018 年央推計） 出所：スリランカ中央銀行（Annual Report 2018）
首都	スリ・ジャヤワルダナプラ・コッテ
言語	シンハラ語、タミル語、英語
宗教	仏教 70.2%、ヒンドゥー教 12.6%、イスラム教 9.7%、キリスト教 6.1% 出所：2012 年センサス
公用語	シンハラ語、タミル語

1.3 調査項目

本調査の調査項目は、表 1-3 のとおりである。

表 1-2：調査項目

No	調査項目
1	医薬品および医療機器の定義および分類
2	医薬品および医療機器の承認等（認証を含む。）に関する規制（承認制度、申請資料の信頼性保証の仕組みを含む。）の内容、およびその動向 について
3	医薬品および医療機器の市販後の安全対策（副作用情報の収集・分析・医療現場への情報提供の方法（含む添付文書改訂）や体制、不良品の回収、偽造品等）に関する規制の内容、およびその動向
4	医薬品および医療機器の製造・品質管理に関する規制（GMP、QMS、薬局方等）の内容、およびその動向
5	医薬品および医療機器の非臨床試験の実施方法等に関する規制（GLP 等）の内容、およびその動向
6	医薬品および医療機器の臨床試験（治験）の実施方法等に関する規制（GCP 等）の内容、およびその動向
7	医薬品および医療機器の副作用等の被害救済に関する制度の内容、およびその動向
8	医薬品・医療機器の販売規制（医師の処方せんの必要性、入手可能な店舗および交付者に関する規制）に関する制度の内容、およびその動向
9	医薬品および医療機器の開発方針、必要な試験の内容、試験計画等に関する相談の仕組み、その内容および動向

1.4 調査手法

インターネットで公開されている関連の文書、資料、公表文献等（日本語、英語）から調査を実施。

第 2 章 スリランカにおける医薬品及び医療機器にかかる規制および所管官庁

2.1 医薬品及び医療機器にかかる規制

2015 年以前は医薬品及び医療機器の輸入・登録を所管していたのは化粧品医療機器薬品機関（Cosmetics, Devices and Drugs Authority：CDDA）であったが、CCDA の後継機関として、スリランカ医薬品規制機関（National Medicines Regulatory Authority：NMRA）が 2015 年 7 月 1 日に設立された。NMRA の設立により、CDDA に関連するすべての法律や規制は 2015 年 6 月 30 日に廃止された。

2.2 スリランカ医薬品規制機関（NMRA）の概要

CDDA とは異なり、NMRA は保健・栄養・伝統医学省大臣に対して直接の説明責任を持つ独立機関として機能するように設立された。NMRA は議長を含む 13 名のメンバーから構成され、(i) 医薬品規制部門（Medicines Regulatory Division：MRD）や（ii）医療機器規制部門（Medical Devices Regulatory Division：MDRD)、(iii) ボーダーライン製品規制部門（Borderline Products Regulatory Division：BPRD）を含む 10 の部門を有している。

医薬品、医療機器、ボーダーライン製品の規制を主管する分科会が、それぞれ医薬品評価委員会（Medicines Evaluation Committee：MEC)、医療機器評価委員会（Medical Devices Evaluation Committee：MDEC)、ボーダーライン製品評価委員会（Borderline Products Evaluation Committee：BPEC）である。

これらを含むすべての分科会を監督しているのが国家助言委員会（National Advisory Committee）であり、13 名のメンバーから成る NMRA に対し、NMRA 法に従った運営方法について助言を与えている。

2.3 CDD 法と NMRA 法

CDD 法と NMRA 法の主な違いは、次のとおりである。CDD 法では薬品と医療機器をその効能、安全性、品質に基づき規制していたが、NMRA 法ではそれらに加えて価格も重要な評価要素の 1 つとしている。これは中所得国であるスリランカが、費用対効果の高いヘルスケア市場の整備を企図しているためである。

第 3 章 医薬品に関する規制

3.1 医薬品の定義及び分類

3.1.1 医薬品の定義

「スリランカ医薬品規制機関（National Medicines Regulatory Authority ： NMRA）法 2015 年 5 号」では、医薬品の定義を以下のように定めている。[1]

1. 人間又は動物の病気や異常な身体的状態の診断、治療、緩和、或いは予防。人間又は動物の臓器の機能の回復、修正の為に製造、販売、又は提供される物質又は物質の混合物。
2. 特別な名称で、又は特徴的な形状で、特許及びそれ以外の（非占有的な）準備が整い製品化され、市場に出されている医薬品又は医薬品の組合わせ。
3. 薬草エキスから作られた製品。
4. 治療的効果を伴う栄養補助食品。
5. ワクチン及び血清。※ アーユルヴェーダ及びホメオパシーは含まれない。

3.1.2 医薬品の分類

スリランカ官報 No. 2145/1（2019 年 10 月）において、医薬品の分類を以下のように定めている。[2]

- スケジュールI：
  ① 処方箋及び当局からのライセンス無しで販売される可能性のある医薬品。
  ② 製造元の未開封の容器又はパックでのみ販売されている医薬品。
  ③ スリランカにおける通常の保管条件の下で安定している事が証明されている医薬品。
- スケジュールIIグループ A：
  当局によって認可された小売薬局で雇用されている薬剤師以外が販売してはならない医薬品。処方箋無しで販売されるケースもある。
- スケジュールIIグループ B, C 及びスケジュールIII：
  当局の認可を受けた小売薬局で雇用されている薬剤師のみが有効な処方箋で販売する医薬品。

表 1-3：分類毎の登録医薬品数（NMRA の HP より）[3]

	I	IIA	IIB	IIC	III
登録数	18	130	6,277	1	12

[1] http://www.nmra.gov.lk/images/PDF/Legislation/5e_nmdra_07.pdf
95/98 頁 18 行目 “medicine” means～96/98 頁 7 行目

[2] http://www.nmra.gov.lk/images/PDF/gazzet/PG--4687--E.pdf
4/68 頁 20 行目 10. (1) At the time of registration, ～5/68 頁 5 行目

[3] https://www.nmra.gov.lk/index.php?option=com_drugs&view=drugs&Itemid=221&lang=en
分類毎の登録数をカウント

3.2 医薬品の承認等（認証を含む）に関する規制（承認制度、申請資料の信頼性保証の仕組みを含む）の内容及びその動向について

スリランカ医薬品規制機関（NMRA）法に基づき設立された医薬品評価委員会（MEC）は、医療及び製薬関連の様々な専門分野から選ばれた専門家で構成されており、医薬品の販売申請に対する決定を行い、医薬品の販売承認に関連するポリシー決定を行う為の会議を毎月開催している。

3.2.1 医薬品の承認

医薬品の承認及び登録に関しては、「スリランカ医薬品規制機関（National Medicines RegulatoryAuthority : NMRA）法 2015 年 5 号」において以下のように定めている。[4]

- 医薬品を製造又は輸入しようとする者は、当局に指定された形式でその医薬品の登録申請を行うものとする。
- 申請書と併せて医薬品の詳細情報、サンプル、所定の費用を提出しなければならない。
- 当局は、医薬品の登録の為に受取った全ての申請を記録する登録簿を維持するものとする。
- 当局は申請書の受領後、その申請書と医薬品のサンプル及び入手可能な全ての詳細情報を提出しなければならない。
  - ① 医薬品評価委員会（Medicine Evaluation Committee : MEC）に対して、医薬品及びアプリケーションの評価の為に提出。
  - ② 国家医薬品品質保証研究所（National Medicines Quality Assurance Laboratory : NMQAL）に対して、医薬品の品質検査の為に提出。
- 当局は、申請書が評価及び試験の為に受領及び提出された事を書面で申請者に通知するものとする。
- 大臣は規制を行う事ができる。
  - ① MEC 及び NMQAL がそれぞれの評価及びテストプロセスで従う手順を指定する。
  - ② 指定内容は、
    - ・試験又は評価を実施する際の期限。
    - ・MEC が会議を実施する方法及び会議において従うべき手順。
    - ・提出する報告書に含めるべき事項。
- 当局は、MEC 及び NMQAL に対して、国民の健康に対する医薬品の緊急性を考慮して、特定の期間内に医薬品の評価又は試験を完了する事を要求する場合がある。
- 当局は必要に応じて、MEC 及び NMQAL によって提出された報告書に関して、MEC, NMQAL 又はその他の専門家に説明を求める事ができる。
- 当局は MEC, NMQAL 及びその他全ての報告を考慮して、規定の期間内に医薬品を登録するか、或いは登録を却下する事ができる。

[4] http://www.nmra.gov.lk/images/PDF/Legislation/5e_nmdra_07.pdf
38/98 頁 1 行目～42/98 頁

■手順

ステップ 1-医薬品の登録に関する新メーカーの承認

製造業者は申請書を提出し、承認を得る必要がある。 製造業者が外国の場合、製造業者を代表する権限を与えられた現地企業を任命し、すべての申請書は現地代理店を通じて提出しなければならない。

製造業者の承認時に、該当する製造業者によって製造された医薬品の登録申請書を提出する必要がある。

ステップ 2-医薬品の登録

申請の種類：医薬品は、承認申請を提出するために、次のカテゴリに大きく分類される。[5]

① New Molecular Entities（NME）：
以前に承認された有効成分を含む、スリランカで以前に登録されていない化学成分。

② New Dosage Forms（NDF）：
スリランカで利用可能な登録済みの医薬品と物理的に異なる剤形の医薬品。

③ New Fixed Dose Combination Products（NCP）：
スリランカで以前に登録されていない、単一の剤形で 2 つ以上の医薬品を含む製剤。

④ バイオ製品及びバイオテクノロジー製品：
・ワクチンと血清（※民間部門でのワクチンの取り扱いと保管のガイドライン参照）
・プラズマ製品
・バイオテクノロジー製品
・その他の生物学的製剤

⑤ New Product of Existing Drugs（NP）：
スリランカで既に登録されている医薬品の新製品。
※承認制度においてジェネリックの区分無し（NP として扱われる）

⑥ 再登録

[5] https://nmra.gov.lk/images/PDF/draft_guidelines/Guideline-on-registration-of-medicine.pdf 8/60 頁 4. CATEGORIES OF APPLICATIONS FOR REGISTRATION

■基本的なフロー

- 医薬品の登録に関するガイドライン（2019 年 10 月）において、医薬品の登録のフロー及び医薬品の登録に関わる詳細事項が示されている。[6]

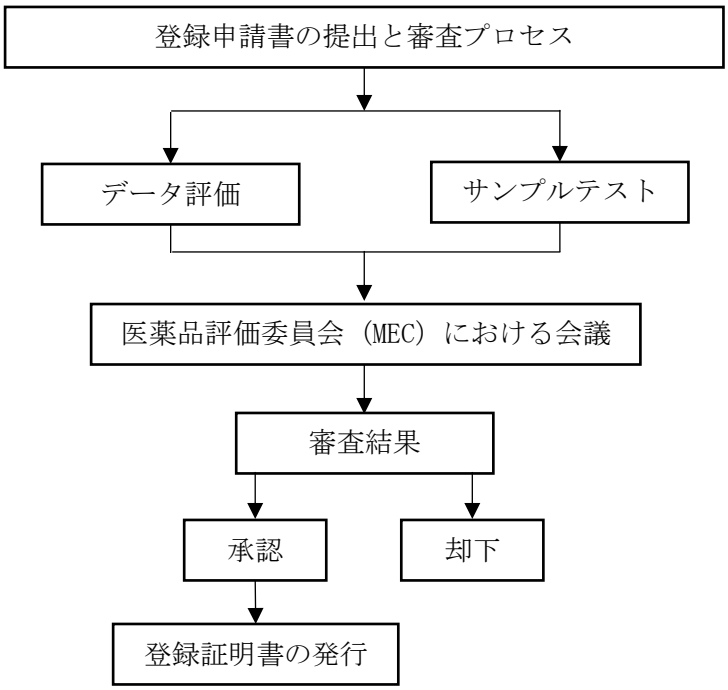


図 1-1：医薬品の登録フロー

[6] https://nmra.gov.lk/images/PDF/draft_guidelines/Guideline-on-registration-of-medicine.pdf 8/60 頁 フロー図

- 申請者は、スリランカに恒久的な住所を有し登記された法人であり、その製造施設がNMRAによるGMPのコンプライアンスについて承認されている必要がある。[7]
- 申請方法は、Webベースのオンライン提出。[8]
- 費用は、NMRA法に基づいて公表された規則No. 2052/33（2018年）に基づく。[9]
- 登録の為に提出された申請書は、当局への提出日に従って時系列に審査され、申請者は、当局への提出後28営業日以内に評価結果が通知される。[10]
- 製品登録証明書は5年間有効であり、申請者は期日前6ヵ月以内に再登録を申請する必要がある。[11]

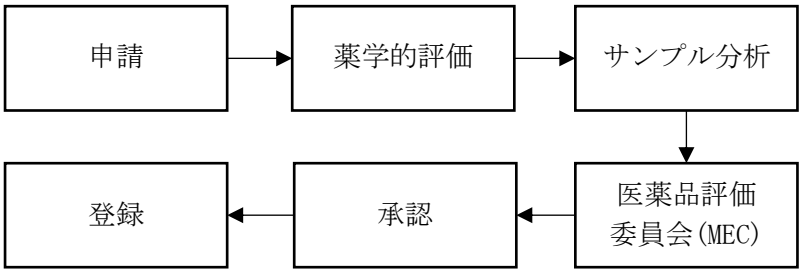


図 1-2：新製品(NP)の登録

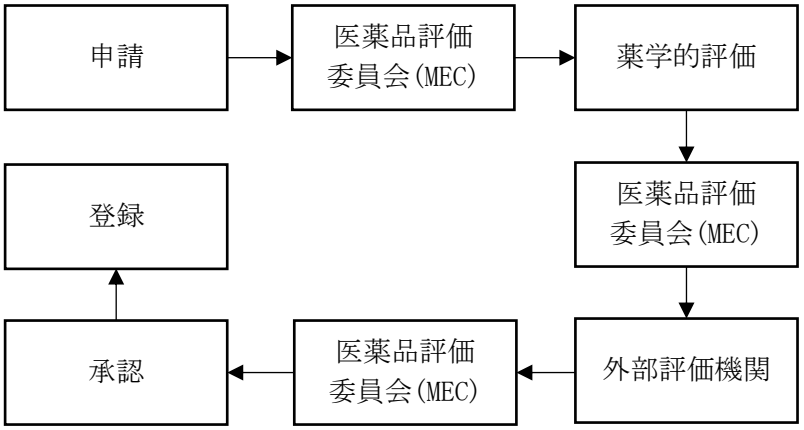


図 1-3：新しい成分(NME)、新しい剤形(NDF)及び新しい組合わせの製品(NCP)の登録
※薬学的評価：生体内評価、発がん性評価、発生毒性評価等

[7] https://nmra.gov.lk/images/PDF/draft_guidelines/Guideline-on-registration-of-medicine.pdf 8/60頁 5. WHO CAN APPLY FOR REGISTRATION OF MEDICINES?

[8] https://nmra.gov.lk/images/PDF/draft_guidelines/Guideline-on-registration-of-medicine.pdf 9/60頁 6. HOW TO APPLY

[9] https://nmra.gov.lk/images/PDF/draft_guidelines/Guideline-on-registration-of-medicine.pdf 9/60頁 7. FEES

[10] https://nmra.gov.lk/images/PDF/draft_guidelines/Guideline-on-registration-of-medicine.pdf 9/60頁 8. EVALUATION AND NOTIFICATION

[11] https://nmra.gov.lk/images/PDF/draft_guidelines/Guideline-on-registration-of-medicine.pdf 55/60頁 本文1～2行目

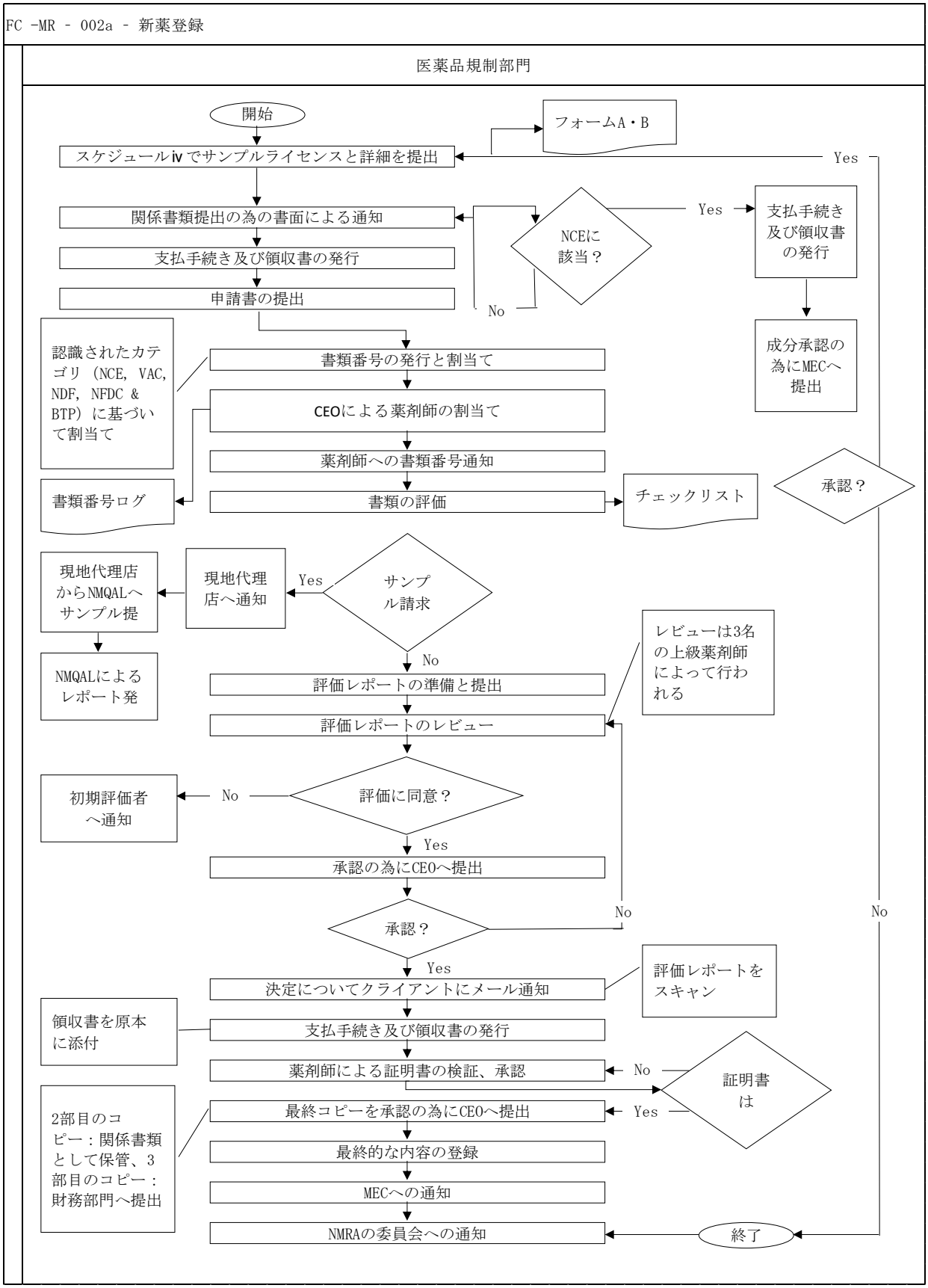


図 1-4：新製品登録フローチャート

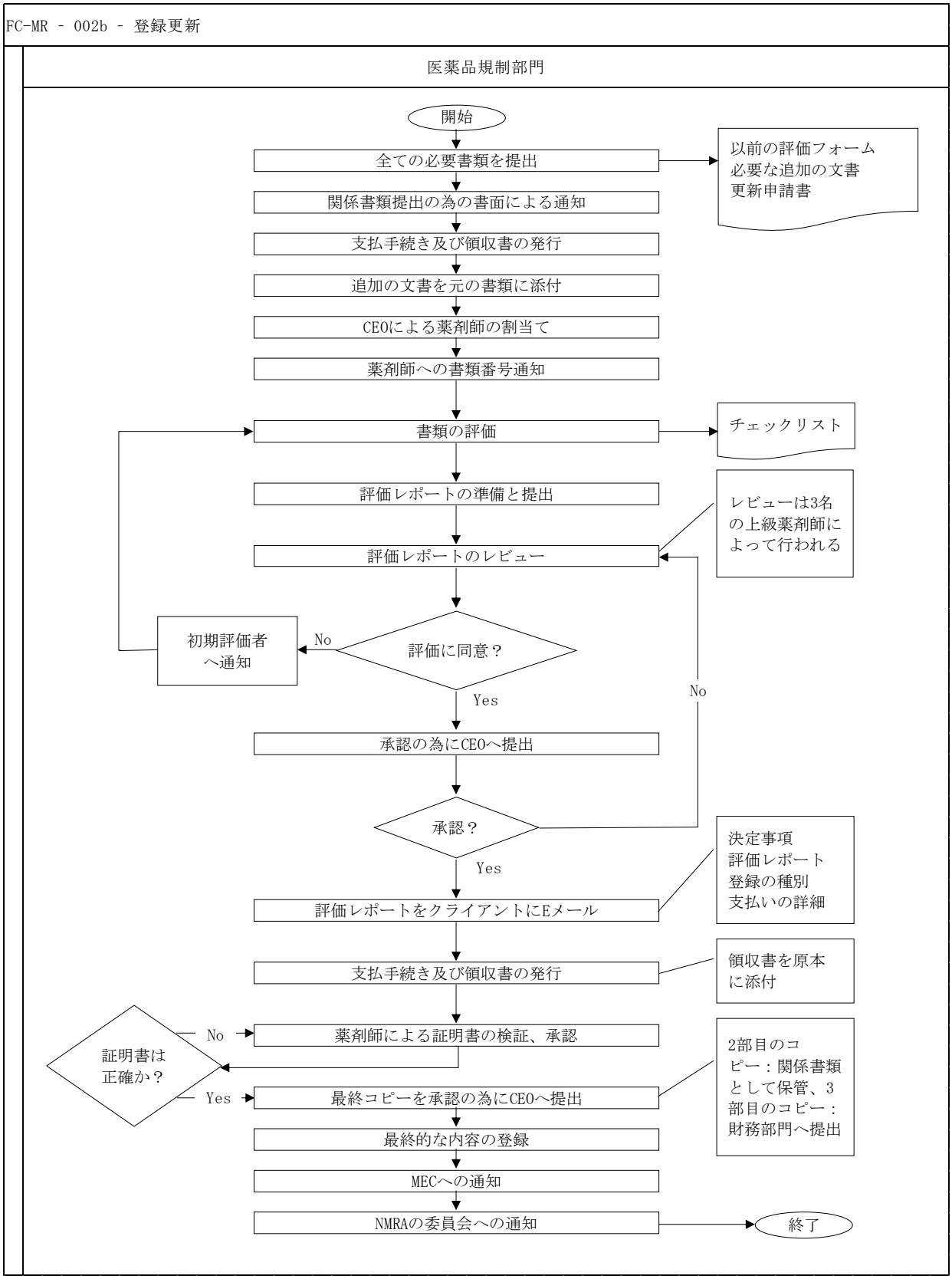


図 1-5：登録更新手続きフローチャート

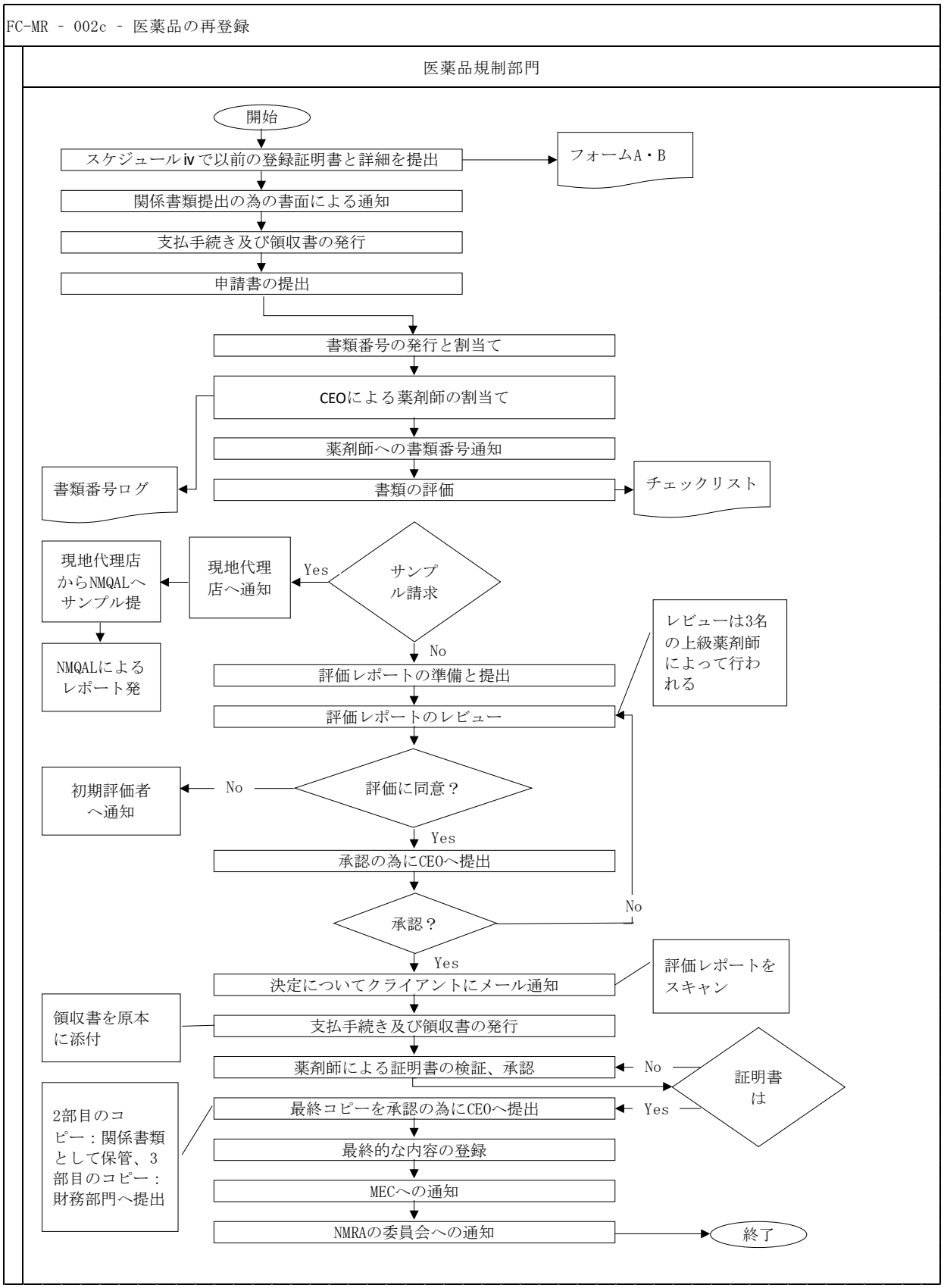


図 1-6：再登録フローチャート

■輸入ライセンスの取得

医薬品の販売承認申請者は、販売承認申請とともに、スリランカで販売する予定の市販パックを最低 2 パックを提出する必要がある。製造業者が海外の場合、そのような登録サンプルを輸入する際に通関を容易にするために NMRA からのサンプルライセンスが必要となる。

以下の書類は、登録サンプルの輸入のための申請書（フォーム C スケジュール V）とともに申請者から提出される必要がある。

- 申請者によるサンプルライセンスのリクエストレター
- 申請者が現地代理人であることを示す製造業者による許可書
- NMRA による製造サイトの承認書（CP 承認書）

NMRA は、特定の製品に対するサンプルライセンスの発行を拒否する権利を留保する。現在、特定の品目の登録製品が 20 個以上ある場合、NMRA は申請を受け付けていない。申請者がサンプルライセンスを取得すると、関連する規制で指定されているライセンスの条件に従う必要がある。特に、申請者は、このようなサンプルライセンスで輸入された商品に関するすべての記録を保持する必要がある。

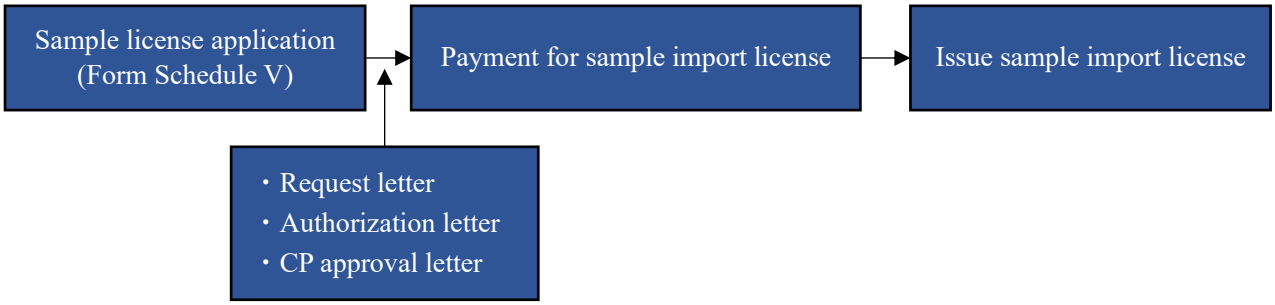


図 1-7：輸入品の登録のサンプル

Regulation 59 (1)

Schedule XI

APPLICATION FOR LICENCE TO IMPORT A MEDICINE AS SAMPLES FOR TEST/ EXAMINATION/ANALYSIS/CLINICAL TRIAL/DISTRIBUTION AS PHYSICIANS SAMPLES

I/We …… of …….. hereby apply for a licence to import from ……

the medicine specified below as samples for the purpose of test/ examination/analysis/clinical trial/distribution as physicians samples.

Generic name of the medicine :……

Brand name (if any):……..

Dosage form and Strength:……

Quantity:……..

Signed: ……..

Regulatory Affairs Officer

Name: ……

Date: ……..

図 1-8：輸入のための申請書（フォーム C スケジュール V）

3.3 医薬品の市販後の安全対策（副作用情報の収集・分析・医療現場への情報提供の方法（含む添付文書改訂）や体制、不良品の回収、偽造品等）に関する規制の内容及びその動向について

■医薬品の市販後の安全対策

- 「スリランカ医薬品規制機関（National Medicines Regulatory Authority : NMRA）法 2015 年 5 号」において、 NMRA が医薬品及び医療機器の品質、安全性、有害反応に関するマーケティング後の監視を実施する旨の記述がある。[12]
- 医薬品安全性監視に関するガイドライン（2019 年 10 月）は、NMRA を含む全ての利害関係者、研究所、及びその役割に関する報告書を提出する個人にガイダンスを提供する。[13]
- 同ガイドラインの提示する個別ケース報告用のフォーマットは、副作用症例報告の適切な評価に必要な情報を収集するように設計されている。 フォーマットに記入する情報は、次の見出しに分類できる。[14]
  ・患者に関する情報
  ・疑わしい医薬品に関する情報
  ・副作用の説明
  ・副作用の管理に関する情報
  ・報告者に関する情報
- アナフィラキシー反応の疑いに関する副作用レポートにおいて頻発するデータの欠落を防止する為に、医薬品安全性監視部門は全ての重要なデータを収集するアナフィラキシーのレポート用に別のフォーマットを導入している。[15]

[12] http://www.nmra.gov.lk/images/PDF/Legislation/5e_nmdra_07.pdf
4/98 頁 19 行目 (j)

[13] https://nmra.gov.lk/images/PDF/guideline/Guideline-on-Pharmacovigilance.pdf
3/12 頁 8 行目 This document provides～9 行目

[14] https://nmra.gov.lk/images/PDF/guideline/Guideline-on-Pharmacovigilance.pdf
6/12 頁 9～16 行目

[15] https://nmra.gov.lk/images/PDF/guideline/Guideline-on-Pharmacovigilance.pdf
6/12 頁 17～19 行目

- 医薬品の市販後調査に関するガイドライン（2019 年 10 月）の主な内容は以下の通り。

  現場の検査担当者と国家医薬品品質保証研究所（National Medicines Quality Assurance Laboratory :NMQAL）は、確認済みのデータが入手可能になり次第、NMRA に結果を報告する必要がある。[16]

  NMRA に提示されたデータと調査結果の潜在的な公衆衛生の重要性に応じて、当局はサンプルの更なるテスト、市場認可保有者からの追加情報又は説明の要求、又はリコールを含むその他の適切な規制措置を講じる。

  NMRA は他の利害関係者、関連グループ、一般市民と結果を共有する。NMRA は、医療用品管理情報システム（MSMIS）を介して政府の医療機関と市販後調査サンプルの結果を共有している。また、市販後監視プログラムからの結果は、オンラインで公開されている NMRA Web サイトを通じて取得できる。

  医師、歯科医、薬剤師、看護師等の医療専門家は、日々の診療で遭遇する疑わしい有害事象を報告するよう奨励されている。[17]

  医薬品の有害事象は、NMRA Web サイトで入手可能な関連フォームに記入する事により、NMRA に報告できる。

  有害事象報告用の NMRA データベースは、承認された全ての医薬品に関する NMRA の市販後安全性監視プログラムをサポートするように設計されたコンピューター化された情報データベースである。

  これらのレポートは、安全性シグナルを検出し、薬物の安全性を監視する為に、学際的なスタッフ（薬理学者、免疫学者、医師等）で構成される安全性及びリスク評価小委員会（SAFREC）によって評価される。

  その結果、NMRA は製品のラベル情報の更新、承認決定及び製品のリコールの再評価等、製品の安全性を向上させ、公衆衛生を保護する規制措置を講じる。

[16] https://nmra.gov.lk/images/PDF/guideline/Guideline-on-Post-Marketing-Surveillance.pdf 7/8 頁 7. DATA ANALYSIS AND REPORTING

[17] https://nmra.gov.lk/images/PDF/guideline/Guideline-on-Post-Marketing-Surveillance.pdf 7/8 頁 8. ADVERSE EVENTS OF MEDICINES

- 即時警告システムに関するガイドライン（2019 年 10 月）の主な内容は以下の通り。[18]

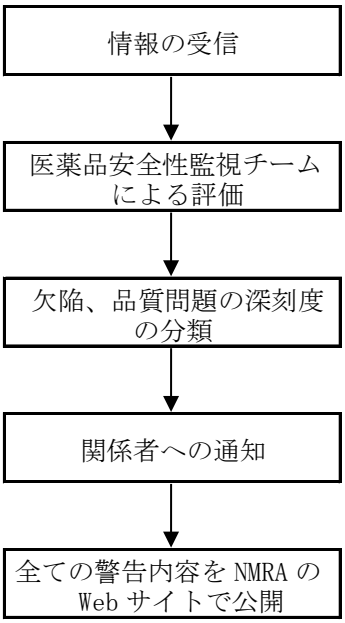


図 1-9：即時警告システムに関するガイドライン NMQAL、政府及び私立病院、WHO、国家規制当局より

クラスI：24 時間以内（電話、SMS, ファックス、メール）（※）
クラスII：24 時間以内、最大 72 時間（電話、SMS, ファックス、メール）
クラスⅢ：迅速な警告システムを介して通知する必要は無し。

（※）
クラスI：生命を脅かす可能性、或いは健康に重大なリスクを引起こす可能性がある場合。
Ex. 間違った製品（ラベルと中身が異なる）
正しい製品だが効力に問題がある製品（深刻な医学的結果を伴う）
クラスII：病気や健康被害を引起こす可能性がある場合。
Ex. 誤表示（文章や図の欠落）
医学的結果を伴う非注射、非眼科滅菌製品の微生物汚染
クラスIII：健康に重大な被害を及ぼす事は無いが、他の事由によって警告の必要がある場合。
Ex. 欠陥のあるパッケージ（バッチ番号や有効期限の誤り又は欠落）不完全な包装

- リコールに関するガイドライン（2019 年 10 月）では、NMRA による正式な指示に応じて、リコールが行われる場合がある。製造業者又はその認可された現地代理店も、製造又は販売された品目に関連する欠陥を特定した場合、自主回収を要求するものとしている。[19]

[18] https://nmra.gov.lk/images/PDF/guideline/Guideline-on-Rapid-alert-system-.pdf
4/8 頁 6. PROCEDURE
[19] https://nmra.gov.lk/images/PDF/guideline/Guideline-on-Recall.pdf
3/7 頁 2. SCOP

3.4 医薬品の製造・品質管理に関する規制（ＧＭＰ、ＱＭＳ、薬局方等）の内容及びその動向について

スリランカ医薬品規制機関（NMRA）において、医薬品・医療機器の GMP に関するガイドラインが制定されている（2019 年 10 月施行)。GMP は品質保証の一部であり、製品が一貫して生産され、使用目的に適した品質基準に管理されている事を保証する。

GMP のコンプライアンスを評価する為に、全ての地元の医薬品製造施設は 2 年に 1 回以上検査している。

海外の製造業者については、特定の製品を生産する際に GMP に準拠した運用がなされている事を、当該国の所管官庁が証明する必要がある。

海外メーカーの GMP 検査の基準と手法は、現在開発中（開発内容の詳細は不明)。

薬局方としてスリランカ独自の公定書は現在存在しない。必要に応じて英国薬局方、米国薬局方を適用しており、日本薬局方は非適用である。（輸出に際しては、輸出先の採用している薬局方の品質規格への適合を確認するが、スリランカから日本へ医薬品を輸出するケースは殆ど無いと考えられる。）

■医薬品の製造・品質管理

- 「スリランカ医薬品規制機関（National Medicines Regulatory Authority : NMRA）法 2015 年 5 号」に基づき、医薬品の GMP に関するガイドライン（2019 年 10 月）が制定されている。同ガイドラインの GMP に関する主な内容は以下の通り。[20]
  - 生産業務は、高品質な製品を供給する事を目的として、製造及び販売承認に従って明確に定義された手順に従う必要がある。[21]
  - 原料受入れと洗浄、検査、サンプリング、保管、調剤、処理、包装、発送等の材料及び製品の全ての取扱いは、書面による手順又は指示に従って行われ、必要に応じて記録される。
  - 指示又は手順からの逸脱は可能な限り避ける必要がある。逸脱が発生した場合、承認された手順[4]に従わなければならない。品質管理部門の関与により、指定された人物が書面で承認する必要がある。従わなければならない。品質管理部門の関与により、指定された人物が書面で承認する必要がある。
  - 歩留まりの確認と数量の調製は、許容範囲外の矛盾が無い事を確認する為に、必要に応じて実行する必要がある。
  - 異なる製品の処理は、混合又は相互汚染のリスクを回避する為、同じエリアで同時に又は連続して実行してはならない。
  - 処理中は常に全ての材料、バルクコンテナ、主要機器、使用しているエリアと包装ラインにラベルを付けるか、処理中の製品又は材料の効力を明記する必要がある。
  - 生産施設へのアクセスは、許可された人員に制限する必要がある。
  - 通常、非医薬品は、医薬品の生産を目的とするエリア又は設備で生産されるべきではない。
  - 工程内管理は通常、生産エリア内で実行される。工程内管理の実行は、当該製品又は別の製品の品質に悪影響を及ぼしてはならない（相互汚染又は混合等)。

[20] http://www.nmra.gov.lk/images/PDF/Legislation/5e_nmdra_07.pdf
33/98 頁 14 行目

[21] https://nmra.gov.lk/images/PDF/guideline/Guideline-on-GMP.pdf
37/44 頁 16. GOOD PRACTICES IN PRODUCTION

- 同ガイドラインによれば、各メーカーには品質管理機能が必要である。品質管理機能は、他の部門から独立し、適切な資格と経験を持つ人物の権限の下になければならない。全ての品質管理機能が効果的かつ確実に実行されるように、適切なリソースが利用可能でなければならない。品質管理の基本要件は以下の通り。[22]
  - 出発材料、包装材料、中間製品、バルク製品、完成製品のサンプリング、試験の為に、GMP 目的の環境条件の監視に適切な施設、訓練された要員、承認された手順が利用可能でなければならない。
  - 出発材料、包装材料、中間製品、バルク製品、最終製品のサンプルは、品質管理部門によって承認された方法と人員によって採取されなければならない。
  - 適格性評価及びバリデーション。
  - 必要な全てのサンプリング、試験手順が実行され、逸脱が完全に記録及び調査された事を実証する記録を作成しなければならない。
  - 最終製品には、販売承認に記載されている製品の定性的及び定量的組成に適合する成分が含まれている必要がある。成分は適切にラベル付けされた適切な容器に入れられ、要求される純度でなければならない。
  - 材料及び中間製品、バルク製品、完成品を仕様に照らして検査及びテストした結果の記録を作成する必要がある。製品評価には、関連する生産文書のレビューと評価、指定された手順からの逸脱の評価を含める必要がある。
  - 出発材料と製品の十分なサンプルを保持し、必要に応じて製品の将来的な検査を受入れる必要がある。保持された製品は、パッケージが非常に大きい場合を除き、最終パッケージに適切な期間保管する必要がある。パッケージが非常に大きい場合は、市販の包装システムと同等のものを使用できる。
  - 薬局方としてスリランカ独自の公定書は現在存在しない。必要に応じて英国薬局方、米国薬局方を適用している。

[22] https://nmra.gov.lk/images/PDF/guideline/Guideline-on-GMP.pdf
40/44 頁 17. GOOD PRACTICES INQUALITY CONTROL

3.5 医薬品の非臨床試験の実施方法等に関する規制（ＧＬＰ等） 3 の内容及びその動向について

■医薬品の非臨床試験

- OECD ガイドラインに基づいて制定された、スリランカ認定委員会（SLAB）による GLP の基準（2015 年 10 月）。SLAB による GLP の基準は、OECD ガイドラインの解釈を提供し、OECD の条項の特定の要件を説明している。[23]
- 同基準は医薬品や農薬製品、化粧品、動物用医薬品、食品添加物、飼料添加物、工業用化学物質等の非臨床安全性試験に適用される。[24]
- 同基準は、以下の 13 章及び添付資料で構成される。[25]
  - ・第 1 章 ： 序章
  - ・第 2 章 ： 認定の範囲
  - ・第 3 章 ： 用語と定義
  - ・第 4 章 ： 試験施設の組織と職員
  - ・第 5 章 ： 品質保証プログラム
  - ・第 6 章 ： 施設
  - ・第 7 章 ： 装置、材料及び試薬
  - ・第 8 章 ： 試験システム
  - ・第 9 章 ： 試験及び参照項目
  - ・第 10 章 ： 標準的な作業手順
  - ・第 11 章 ： 調査の実施
  - ・第 12 章 ： 調査結果の報告
  - ・第 13 章 ： 記録及び資料の保管
  - ・添付資料 ：
    認定の範囲に関する詳細
    GLP 研究要員の能力要件
    技術諮問委員会の構成

[23] http://www.slab.lk/Support/Publications/RECOGNITION_OF_GOOD_LABORATORY_PRACTICE_(GLP)/GLP-GL-(P)-02-SPECIFIC-CRITERIA-02.pdf
3/14 頁 1.4

[24] http://www.slab.lk/Support/Publications/RECOGNITION_OF_GOOD_LABORATORY_PRACTICE_(GLP)/GLP-GL-(P)-02-SPECIFIC-CRITERIA-02.pdf
3/14 頁 1.4

[25] http://www.slab.lk/Support/Publications/RECOGNITION_OF_GOOD_LABORATORY_PRACTICE_(GLP)/GLP-GL-(P)-02-SPECIFIC-CRITERIA-02.pdf
2/14 頁

3.6 医薬品の臨床試験（治験）の実施方法等に関する規制（ＧＣＰ等）の内容及びその動向について

医薬品規制調和国際会議（The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use : ICH）による GCP のガイドラインに基づく臨床試験実施の為のガイドラインを制定（2019 年 10 月施行）。

臨床試験の実施に必要な承認、臨床試験実施の承認申請、個人を臨床試験の参加者として使用する為に必要な同意、試験参加者に説明及び情報を提供する義務、試験材料の詳細、臨床試験の記録等の項目で構成されている。

■医薬品の臨床試験

- 「スリランカ医薬品規制機関（National Medicines Regulatory Authority : NMRA）法 2015 年 5 号」において、スリランカで行われる臨床試験に関連する全ての側面の規制と管理を担当する臨床試験規制部門を設ける旨の記述がある。[26]
- 医薬品規制調和国際会議（The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use : ICH）による GCP のガイドラインに基づく臨床試験実施の為のガイドラインを制定している（2019 年 10 月）。[27]
- 同ガイドラインは、以下の 7 章及び添付資料で構成される。
  - ・第 1 章 ： 目的
  - ・第 2 章 ： 範囲
  - ・第 3 章 ： 手順
    1. 臨床試験の実施に必要な承認
    2. NMRA によって承認された倫理審査委員会
    3. 臨床試験評価委員会（CTEC）の承認を必要とする臨床試験のカテゴリー
    4. スリランカでの実施が許可されている臨床試験の段階
    5. 臨床試験を実施する為の承認申請
    6. 臨床試験の優先審査
    7. 関連プロセスのスケジュール
    8. CTEC への定期報告
    9. 臨床試験の安全性報告要件添付資料 ：
       CIOM-I format
       重篤な副作用の緊急報告書に含まれるデータ要素
       CTEC への臨床試験の安全性報告要件とスケジュール
  - ・第 4 章 ： 定義
  - ・第 5 章 ： 関連する法律及び文書
  - ・第 6 章 ： フィードバック
  - ・第 7 章 ： 承認とレビュー

[26] http://www.nmra.gov.lk/images/PDF/Legislation/5e_nmdra_07.pdf
22/98 頁 9 行目

[27] https://nmra.gov.lk/images/PDF/guideline/Guideline-for-GCP-ICH.pdf
https://nmra.gov.lk/images/PDF/guideline/Guideline-for-the-conduct-of-Clinical-Trials-in-Sri-Lanka.pdf
2/18 頁

3.7 医薬品の副作用等の被害救済に関する制度の内容及びその動向について

■医薬品の副作用等の被害救済

- 医薬品・医療機器の副作用等の被害救済に関する制度は無し。現時点において救済制度の制定の動きは見られない。スリランカ医薬品規制機関（NMRA）は、医薬品・医療機器関連規定の整備を進めており、将来的に救済制度が制定される可能性はある。

3.8 医薬品の販売規制（医師の処方せんの必要性、入手可能な店舗及び交付者に関する規制）に関する制度の内容及びその動向について

NMRA による医薬品・医療機器の適正流通に関するガイドライン（2019 年 8 月施行）において、NMRA の関連資料に登録された製品の全ての製造業者、輸入業者、卸売業者は、登録製品及び消費者向けの関連資料の流通と保管に適した適切な流通と保管管理手順を採用する必要があるとされている。

これらの手順には、材料又は製品の安全性と品質を維持する人員・施設の管理と適切な文書化手順が含まれる。

■医薬品の販売規制

- 「スリランカ医薬品規制機関（National Medicines Regulatory Authority : NMRA）法 2015 年 5 号」に基づく薬局業務のガイドライン（2017 年 10 月）において薬局は、小売による医薬品・医療機器の販売の為に NMRA によって発行されたライセンスを保持している施設として定義される。[28]
- 新しい薬局を設立するには、同ガイドラインに含まれる基準と要件を満たす必要がある。既存の薬局も、ライセンスの更新中に要件に準拠する事が期待されている。[29]

[28] http://www.nmra.gov.lk/images/PDF/Legislation/5e_nmdra_07.pdf
68/98 頁 19 行目 120.

[29] http://nmra.gov.lk/images/PDF/guideline/pharmacy_guidelines_2017_dec.pdf
1/9 頁 1. Introduction

- 同ガイドラインの概要は以下の通り。

① 施設

・立地[30]

：薬局は医薬品、医療機器等の提供に適した衛生的な環境に立地する必要がある。

・新規薬局設立の基準[31]

：最も近い薬局からの距離は都市部において 250m 以上、地方部において 750m 以上でなければならない。

・看板と広告[32]

：看板には、薬局の専門的なイメージを投影する必要がある。NMRA が許可するロゴは、簡単に識別できるように表示する必要がある。看板において医薬品の広告は許可されていない。

② 業務

・サービス[33]

：処方箋を取扱う事、薬剤の調合を行う事を必須要件とする。

・商品[34]

：商品の 70%が、登録済みの医薬品、医療機器、健康・栄養商品、パーソナルケア商品等で構成される必要がある。

③ 人材

・薬剤師[35]

：スリランカ医学評議会に登録済みである事。

・サポートスタッフ[36]

：適切な人数である事。スタッフの役割は調剤される医薬品の準備を支援する事であり、スケジュールII～III（医療用）の薬を調剤する事は許可されていない。

④ 保管[37]

：全ての医薬品・医療機器はラベル表示要件に準拠する必要があり、元の状態で保管する必要がある。

[30] http://nmra.gov.lk/images/PDF/guideline/pharmacy_guidelines_2017_dec.pdf 1/9 頁 2. PREMISES 2.1 Location

[31] http://nmra.gov.lk/images/PDF/guideline/pharmacy_guidelines_2017_dec.pdf 1/9 頁 2. PREMISES 2.2 Criteria to establish a new pharmacy (a) Distance

[32] http://nmra.gov.lk/images/PDF/guideline/pharmacy_guidelines_2017_dec.pdf 2/9 頁 2.3 Signboard & Advertisements

[33] http://nmra.gov.lk/images/PDF/guideline/pharmacy_guidelines_2017_dec.pdf 5/9 頁 3. PRACTICE 3.1 Services

[34] http://nmra.gov.lk/images/PDF/guideline/pharmacy_guidelines_2017_dec.pdf 5/9 頁 3. PRACTICE 3.2 Type of products

[35] http://nmra.gov.lk/images/PDF/guideline/pharmacy_guidelines_2017_dec.pdf 5/9 頁 4. Personnel (4.1) Pharmacists

[36] http://nmra.gov.lk/images/PDF/guideline/pharmacy_guidelines_2017_dec.pdf 6/9 頁 4. Personnel (4.2) Pharmacy support staff

[37] http://nmra.gov.lk/images/PDF/guideline/pharmacy_guidelines_2017_dec.pdf 6/9 頁 5. Storage of medicines

- 上記のガイドラインに加え、適正な薬局業務に関するガイドラインが制定されている（2019年10月）。同ガイドラインは主に薬局の構造に関するガイドライン、薬局の運営に関するガイドラインで構成されており、それぞれに含まれる項目は以下の通り。[38]

表 1-4：薬局の構造・運営に関するガイドライン

【薬局の構造に関するガイドライン】

1. 前提条件
2. 家具と備品
3. 設備
4. 人材
5. システム
6. 品質ポリシー
7. サービスポリシー
8. 人材教育ポリシー
9. 苦情ポリシー
10. リコールポリシー
11. 監査ポリシー
12. ドキュメントシステム

【薬局の運営に関するガイドライン】

1. 調達及び在庫管理
2. ストレージ管理
3. 未使用の医薬品及び廃棄物の処分
4. 処方箋の取扱い
5. 調剤
6. 即時調剤
7. 患者向けの情報
8. 患者へのカウンセリング
9. 専門的なガイダンス
10. 投薬記録
11. 患者のフォローアップ
12. セルフケア
13. 健康増進と病気予防
14. 医薬品安全性監視
15. 専門的役割の強化
16 専門家との交流

- 「スリランカ医薬品規制機関（NMRA）法2015年5号」に基づく適正流通に関するガイドライン（2019年8月）[7]において、NMRAの関連資料に登録された製品の全ての製造業者、輸入業者、卸売業者は、登録製品及において、NMRAの関連資料に登録された製品の全ての製造業者、輸入業者、卸売業者は、登録製品及び消費者向けの関連資料の流通と保管に適した適切な流通と保管管理手順を採用する必要があるとされている。[39]
- これらの手順には、材料又は製品の安全性と品質を維持する人員・施設の管理と適切な文書化手順が含まれる。[40]

3.9 医薬品の開発方針、必要な試験の内容、試験計画等に関する相談の仕組み、その内容及び動向について

■医薬品の開発方針等に関する相談

- 開発や試験内容、試験計画に関わる相談についての資料は存在しないが、スリランカ医薬品規制機関（NMRA）は必要に応じて相談を実施していると考えられる。

[38] https://nmra.gov.lk/images/PDF/guideline/Guideline-for-Good-Pharmacy-Practice.pdf 2/14頁

[39] https://nmra.gov.lk/images/PDF/guideline/Guideline-on-Good-Distribution-practices.pdf 3/21頁 本文8～10行目

[40] https://nmra.gov.lk/images/PDF/guideline/Guideline-on-Good-Distribution-practices.pdf 3/21頁 本文11～12行目

第 4 章 医療機器に関する規制

4.1 医療機器の定義及び分類

■医療機器の定義

- 「スリランカ医薬品規制機関（National Medicines Regulatory Authority : NMRA）法 2015 年 5 号」では、医療機器の定義を以下のように定めている。[41]

単一又は組合わせて使用される機器、装置、ソフトウェア、素材、その他の物品。製造業者が意図する適切なアプリケーションに必要なソフトウェアを含む。医療機器は以下の目的において人体の内部或いは人体上で使用される。

① 病気の診断、予防、監視、治療又は緩和。
② 怪我又は障害の診断、監視、治療又は緩和。
③ 解剖学又は生理学的プロセスの調査、修正。

薬理学的、免疫学的又は代謝的手段によって人体内部或いは人体上で意図された作用を達成しないが、上記のような手段によってその機能を支援する事ができる。
※ アーユルヴェーダ及びホメオパシーは含まれない。

■医療機器の分類

- 医療機器の市販後調査計画のフォーマット内でクラスI・クラスIIA・クラスIIB・クラスIIIの 4 段階に分類されており、分類方法についての記述は無いが、国際的な分類（A～D）に従うものと考えられる。なお、分類別内訳は公表されていない。
  ・クラスI（低リスク）
  ・クラスIIA（比較的低リスク）
  ・クラスIIB（比較的高リスク）
  ・クラスIII（高リスク）

表 1-5：登録医療機器数（NMRA の HP より）[42]

登録数	2,103

[41] http://www.nmra.gov.lk/images/PDF/Legislation/5e_nmdra_07.pdf
94/98 頁 24 行目 “medical device” means～95/98 頁 13 行目

[42] https://www.nmra.gov.lk/index.php?option=com_devices&view=devices&Itemid=224&lang=en
登録数をカウント

4.2 医療機器の承認等（認証を含む）に関する規制（承認制度、申請資料の信頼性保証の仕組みを含む）の内容及びその動向について

スリランカ医薬品規制機関（NMRA）法に基づき設立された医療機器評価委員会（MDEC）は、医療及び製薬関連の様々な専門分野から選ばれた専門家で構成されており、医療機器の販売申請に対する決定を行い、医療機器の販売承認に関連するポリシー決定を行う為の会議を毎月開催している。

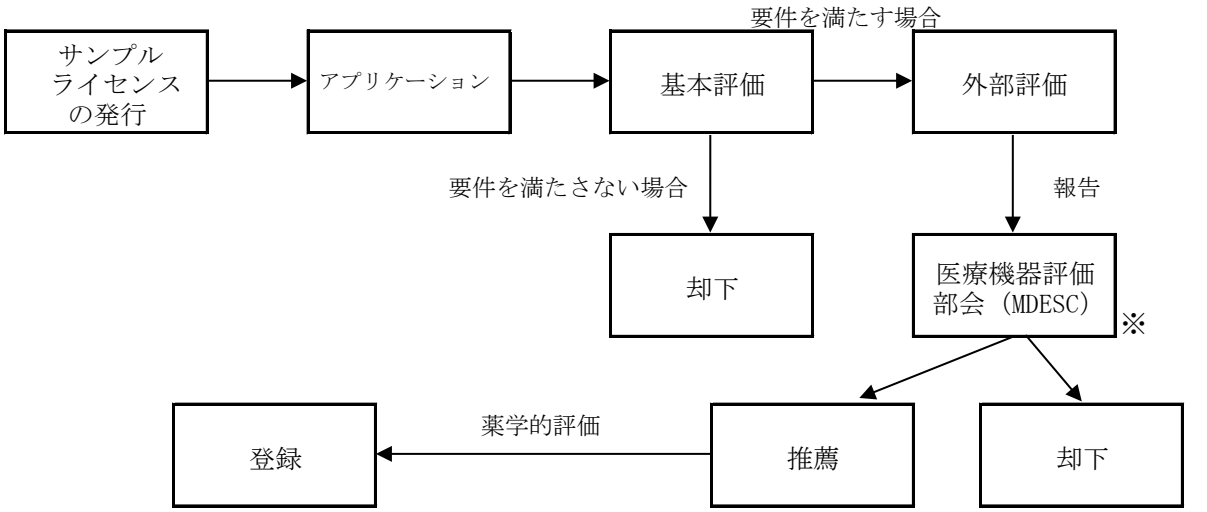
■医療機器の承認

- 医療機器の承認及び登録に関しては、「スリランカ医薬品規制機関（National Medicines Regulatory Authority : NMRA）法 2015 年 5 号」において以下のように定めている。[43]
  - 医療機器を製造又は輸入しようとする者は、当局に所定の形式でその医療機器の登録申請を行うものとする。
  - 申請書と併せて医療機器の詳細情報、サンプル、所定の費用を提出しなければならない。
  - 当局は、医療機器の登録の為に受取った全ての申請が記録される登録簿を維持しなければならない。
  - 当局は申請書を受取り次第、その申請書のコピーと医療機器のサンプル及び入手可能な全ての詳細情報を提出しなければならない。
    ① 医療機器評価委員会（Medical Devices Evaluation Committee : MDEC）に対して、医療機器及びアプリケーションの評価の為。
    ② 国家医薬品品質保証研究所（National Medicines Quality Assurance Laboratory : NMQAL）に対して、医療機器の品質検査の為に提出。
  - 当局は、申請の受領を書面で申請者に通知するものとする。
  - 大臣は規制を行う事ができる。
    ① MDEC 及び NMQAL がそれぞれのテスト又は評価プロセスで従う手順を指定する。
    ② 指定内容は、
    ・試験又は評価を実施する際の期限。
    ・MDEC が会議を実施する方法及び会議で従うべき手順。
    ・提出する報告書に含めるべき事項。
  - 当局は、医療機器の緊急性を考慮して、MDEC 及び NMQAL に指定された期間内に評価又は試験を完了する事を要求する場合がある。
  - 当局は必要に応じて、MDEC 及び NMQAL によって提出された報告書に関して、MDEC, NMQAL 又はその他の専門家に説明を求める事ができる。
  - 当局は MDEC, NMQAL 及びその他全ての報告を考慮して、規定の期間内に医療機器を登録するか、或いは登録を却下する事ができる。

[43] http://www.nmra.gov.lk/images/PDF/Legislation/5e_nmdra_07.pdf
49/98 頁 27 行目 82. (1) No person shall manufacture～52/98 頁 7 行目

- 医療機器の登録に関するガイドライン（2011 年）において、医療機器の登録のフロー及び医療機器の登録に関わる詳細事項が示されている。[44]

【医療機器の登録フロー】



※MDESC ： Medical Device Evaluation Sub Committee

図 1-10：医療機器の登録フロー

- 製造者又は輸入者である申請者/登録所有者は、登録されたデバイスの安全性、品質、及び有効性を確保する責任があり、製品が既存の全ての規制及び仕様（規格）に準拠している事を書面で証明する必要がある。[45]
- デバイスの登録は 5 年間有効であり、有効期限は証明書に記載される。登録の更新は 5 年毎に行われる。特定の状況では、仮登録が 1 年間許可される。[46]

[44] https://nmra.gov.lk/images/PDF/guideline/device_guideline_doc_05.pdf 14/14 頁 フロー図

[45] https://nmra.gov.lk/images/PDF/guideline/device_guideline_doc_05.pdf 4/14 頁 7～9 行目

[46] https://nmra.gov.lk/images/PDF/guideline/device_guideline_doc_05.pdf 13/14 頁 11～12 行目

4.3 医療機器の市販後の安全対策（副作用情報の収集・分析・医療現場への情報提供の方法（含む添付文書改訂）や体制、不良品の回収、偽造品等）に関する規制の内容及びその動向について

スリランカ医薬品規制機関（NMRA）は、医療機器の市販後調査計画のフォーマットを、医療機器関連企業及び医療関係者の便宜の為に公開している。

フォーマットにはレポートの概要、レポートの提出者に関する情報、医療機器に関する情報、事故に関する情報、患者に関する情報、医療施設に関する情報、製造業者のコメント、製造業者の最終調査の結果（最終報告）等の項目が含まれる。

尚、NMRA は市販後医療機器において安全性に問題が生じた場合、事業者に当該医療機器の回収、添付文書の改訂等を指示している。

■医療機器の市販後の安全対策

- 「スリランカ医薬品規制機関（National Medicines Regulatory Authority : NMRA）法 2015 年 5 号」において、 NMRA が医薬品及び医療機器の品質、安全性、有害反応に関するマーケティング後の監視を実施する旨の記述がある。[47]
- NMRA は、医療機器の市販後調査計画のフォーマットを、医療機器関連企業及び医療関係者の便宜の為に公開している。
- フォーマットにはレポートの概要、レポートの提出者に関する情報、医療機器に関する情報、事故に関する情報、患者に関する情報、医療施設に関する情報、製造業者のコメント、製造業者の最終調査の結果（最終報告）等の項目が含まれる。
- 尚、NMRA は市販後医療機器において安全性に問題が生じた場合、事業者に当該医療機器の回収、添付文書の改訂等を指示している。

[47] http://www.nmra.gov.lk/images/PDF/Legislation/5e_nmdra_07.pdf
4/98 頁 19 行目 (j)

4.4 医療機器の製造・品質管理に関する規制（ＧＭＰ、ＱＭＳ、薬局方等）の内容及びその動向について

スリランカ医薬品規制機関（NMRA）において、医薬品・医療機器の GMP に関するガイドラインが制定されている（2019 年 10 月施行）。GMP は品質保証の一部であり、製品が一貫して生産され、使用目的に適した品質基準に管理されている事を保証する。

■医療機器の製造・品質管理

- 「スリランカ医薬品規制機関（National Medicines Regulatory Authority : NMRA）法 2015 年 5 号」において、医療機器の項目で GMP に言及しているが、細目を定めるガイドラインは制定されていない。[48]

4.5 医療機器の非臨床試験の実施方法等に関する規制（ＧＬＰ等） 3 の内容及びその動向について

■医療機器の非臨床試験

- 医療機器に関して GLP の基準は制定されておらず、OECD ガイドラインを適用していると考えられる。

4.6 医療機器の臨床試験（治験）の実施方法等に関する規制（ＧＣＰ等）の内容及びその動向について

医薬品規制調和国際会議（The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use : ICH）による GCP のガイドラインに基づく臨床試験実施の為のガイドラインを制定（2019 年 10 月施行）。

臨床試験の実施に必要な承認、臨床試験実施の承認申請、個人を臨床試験の参加者として使用する為に必要な同意、試験参加者に説明及び情報を提供する義務、試験材料の詳細、臨床試験の記録等の項目で構成されている。

■医療機器の臨床試験

- 医薬品規制調和国際会議（The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use : ICH）による GCP のガイドラインに基づく臨床試験実施の為のガイドライン（2019 年 10 月）は、医療機器に言及しておらず、医療機器の臨床試験に関する規制は運用されていない。

4.7 医療機器の副作用等の被害救済に関する制度の内容及びその動向について

■医療機器の副作用等の被害救済

- 医薬品・医療機器の副作用等の被害救済に関する制度は無し。現時点において救済制度の制定の動きは見られない。スリランカ医薬品規制機関（NMRA）は、医薬品・医療機器関連規定の整備を進めており、将来的に救済制度が制定される可能性はある。

[48] http://www.nmra.gov.lk/images/PDF/Legislation/5e_nmdra_07.pdf
48/98 頁 14 行目 47. (1) The Authority～21 行目

4.8 医療機器の販売規制（医師の処方せんの必要性、入手可能な店舗及び交付者に関する規制）に関する制度の内容及びその動向について

NMRA による医薬品・医療機器の適正流通に関するガイドライン（2019 年 8 月施行）において、NMRA の関連資料に登録された製品の全ての製造業者、輸入業者、卸売業者は、登録製品及び消費者向けの関連資料の流通と保管に適した適切な流通と保管管理手順を採用する必要があるとされている。

これらの手順には、材料又は製品の安全性と品質を維持する人員・施設の管理と適切な文書化手順が含まれる。

■医療機器の販売規制

- 「スリランカ医薬品規制機関（National Medicines Regulatory Authority : NMRA）法 2015 年 5 号」において、「いかなる人も、適正薬局業務及びその他の規定のガイドライン又は条件を遵守せずに医療機器を販売してはならない。」「いかなる人も、適正流通基準及びその他の規定のガイドライン又は条件を遵守せずに医療機器を輸入又は流通してはならない。」と記述されており、医薬品の販売規制において挙げたガイドラインが医療機器にも適用される事が示されている。[49]

4.9 医療機器の開発方針、必要な試験の内容、試験計画等に関する相談の仕組み、その内容及び動向について

■医療機器の開発方針等に関する相談

- 開発や試験内容、試験計画に関わる相談についての資料は存在しないが、スリランカ医薬品規制機関（NMRA）は必要に応じて相談を実施していると考えられる。

[49] http://www.nmra.gov.lk/images/PDF/Legislation/5e_nmdra_07.pdf
48/98 頁 75. (3)
48/98 頁 75. (2)

PARLIAMENT OF THE DEMOCRATIC SOCIALIST REPUBLIC OF SRI LANKA

NATIONAL MEDICINES REGULATORY AUTHORITY ACT, No. 5 OF 2015

[Certified on 19th March, 2015]

Printed on the Order of Government

Published as a Supplement to Part II of the **Gazette of the Democratic Socialist Republic of Sri Lanka** of March 20, 2015

PRINTED AT THE DEPARTMENT OF GOVERNMENT PRINTING, SRI LANKA

TO BE PURCHASED AT THE GOVERNMENT PUBLICATIONS BUREAU, COLOMBO 5

Price : Rs. 100.00 **Postage : Rs. 70.00**

National Medicines Regulatory Authority
Act, No. 5 of 2015

[Certified on 19th March, 2015]

L.D.—O. 21/2012

AN ACT TO PROVIDE FOR THE ESTABLISHMENT OF A REGULATORY AUTHORITY TO BE KNOWN AS THE NATIONAL MEDICINES REGULATORY AUTHORITY WHICH SHALL BE RESPONSIBLE FOR THE REGULATION AND CONTROL OF, REGISTRATION, LICENSING, MANUFACTURE, IMPORTATION AND ALL OTHER ASPECTS PERTAINING TO MEDICINES, MEDICAL DEVICES, BOARDERLINE PRODUCTS AND FOR THE CONDUCTING OF CLINICAL TRIALS IN A MANNER COMPATIBLE WITH THE NATIONAL MEDICINES POLICY; TO PROVIDE FOR THE ESTABLISHMENT OF DIVISIONS OF THE NATIONAL MEDICINES REGULATORY AUTHORITY INCLUDING THE MEDICINES REGULATORY DIVISION, MEDICAL DEVICES REGULATORY DIVISION, BORDERLINE PRODUCTS REGULATORY DIVISION AND CLINICAL TRIALS REGULATORY DIVISION; TO ESTABLISH A NATIONAL ADVISORY BODY; TO REPEAL THE COSMETICS, DEVICES AND DRUGS ACT, NO. 27 OF 1980; AND FOR MATTERS CONNECTED THEREWITH OR INCIDENTAL THERETO.

BE it enacted by the Parliament of the Democratic Socialist Republic of Sri Lanka as follows :-

Short title and date of operation.

1. This Act may be cited as the National Medicines Regulatory Authority Act, No. 5 of 2015 and shall come into operation on such date as the Minister may appoint by Order published in the *Gazette* (hereinafter referred to as "the appointed date").

2—PL 008818—2,950 (02/2015)

CHAPTER I

NATIONAL MEDICINES REGULATORY AUTHORITY

PART I

ESTABLISHMENT OF THE AUTHORITY

Establishment of the National Medicines Regulatory Authority.

2. (1) There shall be established an authority called the National Medicines Regulatory Authority (hereinafter referred to as the 'Authority').

(2) The Authority shall, by the name assigned to it by this section be a body corporate and shall have perpetual succession and a common seal and may sue and be sued in such name.

Objects of the Authority.

3. The objects of the Authority shall be to –

(*a*) ensure the availability of efficacious, safe and good quality medicines, efficacious, safe and good quality medical devices and efficacious, safe and good quality borderline products to the general public at affordable prices;

(*b*) function as the central regulator for all matters connected with the registration, licensing, cancellation of registration or licensing, pricing, manufacture, importation, storage, transport, distribution, sale, advertising and disposal of medicines, medical devices and borderline products;

(*c*) ensure that all activities related to registration, licensing and importation of medicines, medical devices, borderline products and investigational medicinal products are carried out in a transparent, sustainable and equitable manner;

(*d*) encourage the manufacturing of good quality medicines in Sri Lanka with a view to assuring the availability of essential medicines at affordable prices;

(*e*) promote the safe and rational use of medicines, medical devices and borderline products by health care professionals and consumers;

(*f*) recommend appropriate amendments to relevant laws pertaining to medicines, medical devices and borderline products;

(*g*) educate the general public, health care professionals and all stakeholders on medicines, medical devices and borderline products;

(*h*) regulate the promotion and marketing of medicines, medical devices and borderline products;

(*i*) regulate the availability of the medicines, medical devices and borderline products;

(*j*) conduct post marketing surveillance on quality, safety and adverse reaction of the medicines, medical devices and borderline products; and

(*k*) regulate all matters pertaining to the conduct of clinical trials in Sri Lanka.

4. The Authority shall consist of the following :- Constitution of the Authority.

(a) *ex-officio* members –

(i) the Director-General of Health Services;

(ii) the Secretary to the Treasury or his nominee; and

(iii) the Chief Executive Officer of the Authority appointed under section 15 who shall function as the Secretary to the Authority;

(*b*) following persons who shall be appointed by the Minister, (hereinafter referred to as "appointed members") –

(i) four specialist clinicians attached to the Ministry of Health, representing the following clinical disciplines, nominated by their respective professional bodies:-

(A) General Medicine;

(B) General Surgery;

(C) Pediatrics; and

(D) Gynaecology and Obstetrics;

(ii) a Professor in Pharmacology of any University in Sri Lanka established under the Universities Act, No.16 of 1978, appointed in rotation for every three years, in consultation with the respective Deans of Faculties of Medicine;

(iii) a Professor or Senior Lecturer in Pharmacy of any University in Sri Lanka established under the Universities Act, No.16 of 1978, appointed in rotation for every three years, in consultation with the respective Deans of relevant Faculties;

(iv) four professionals, who have gained eminence in the fields of management, law, accountancy or health respectively.

Chairman of the Authority.

5. (1) The Minister shall, in consultation with the Authority appoint one of the appointed members to be the Chairman of the Authority.

(2) The Chairman may resign from the office of Chairman by letter addressed to the Minister and such resignation shall be effective from the date on which it is accepted by the Minister.

(3) The Minister may for reasons assigned remove the Chairman from the office of Chairman.

(4) Subject to the provisions of subsections (2) and (3), the term of office of the Chairman shall be the period of his membership of the Authority.

(5) Where the Chairman is temporarily unable to perform the duties of his office due to ill health, other infirmity, absence from Sri Lanka or any other cause, the Minister may appoint any other appointed member to act as Chairman in addition to his normal duties as an appointed member.

Conflict of interests of the members.

6. (1) The Minister shall, prior to appointing a person as a member of the Authority, satisfy himself that such person has no financial or other conflict of interest in the affairs of the Authority, as is likely to affect adversely, the discharging of his functions as a member of the Authority.

(2) The Minister shall also satisfy himself, from time to time, that no member of the Authority has since being appointed acquired any such interest.

(3) The person to be appointed as a member of the Authority shall be a person who has not been engaged in any employment or assignment in the pharmaceutical industry within the period of three years immediately prior to such appointment.

(4) No person shall engage in any employment or assisgnment in the pharmaceutical industry within the period of three years immediately after such person ceased to be a member of the Authority.

(5) (*a*) A member of the Authority who is in any way, directly or indirectly interested in any contract made or

proposed to be made by the Authority shall disclose the nature of his interest at a meeting of the Authority; and

(*b*) Such disclosure shall be recorded in the minutes of the Authority and the member shall not participate in any deliberation or decision of the Authority with regard to that contract.

(6) Minister may make regulations to further specify and give effect to the provisions of this section.

(7) For the purposes of this section-

"a member of the Authority" includes the Chairman, an appointed member and an *ex-officio* member; and

"conflict of interest" includes any dealing with any company or undertaking which engages in manufacturing, importation, distribution or sale of medicines, medical devices, borderline products or investigational medicinal products.

Disqualifications to be a member.

7. A person shall be disqualified from being appointed or continuing as a member of the Authority, if he –

(*a*) is or becomes a Member of Parliament, any Provincial Council or of any Local Authority;

(*b*) is not, or ceases to be, a citizen of Sri Lanka;

(*c*) directly or indirectly holds or enjoys any right or benefit under any contract made by or on behalf of the Authority;

(*d*) has any financial or other interest as is likely to affect prejudicially the discharge by him of his functions as a member of the Authority;

(*e*) is absent himself from three consecutive meetings of the Authority;

(*f*) is under any law in force in Sri Lanka or any other country, found or declared to be of unsound mind;

(g) is a person who having been declared as insolvent or bankrupt under any law in force in Sri Lanka or in any other country, is an undischarged insolvent or bankrupt; or

(*h*) is serving or has served a sentence of imprisonment imposed by any court in Sri Lanka or any other country.

Ex-officio members.

8. Every *ex-officio* member of the Authority shall hold office so long as such officer holds office by virtue of which such officer has been appointed to the Authority.

Provisions relating to appointed members.

9. (1) Every appointed member of the Authority shall, unless such officer vacates office earlier by death, resignation or removal, hold office for a period of three years, and shall be eligible for re-appointment, unless removed on disciplinary grounds.

(2) The Minister may for reasons assigned remove any appointed member from office.

(3) Any appointed member may resign from office at any time by letter addressed in that behalf to the Minister and such resignation shall take effect upon it being accepted by the Minister.

(4) (*a*) In the event of the death, resignation or removal from office of any appointed member, the Minister may having regard to the provisions of this Act in relation to the appointment of that particular appointed member, appoint another person to act in his place.

(*b*) The Minister shall appoint the member for the purposes of paragraph (*a*) within one month of the occurrence of such vacancy.

(*c*) The member appointed under paragraph (*a*) shall hold office for the unexpired period of the term of office of the member whom he succeeds.

(5) Where any appointed member is temporarily unable to perform the duties of his office due to ill health or absence from Sri Lanka or for any other reason, the Minister may having regard to the provisions of section 4(*b*) appoint another person to act in his place.

(6) Subject to the preceding provisions, an appointed member may continue to hold office, after lapse of the period of three years referred to in subsection (1), until he is reappointed or a new member is appointed by the Minister.

Meetings of the Authority.

10. (1) The Chairman shall preside at every meeting of the Authority. Where the Chairman is absent, the members present shall elect a Chairman for that meeting from among themselves.

(2) (*a*) All matters for decision by the Authority shall be dealt with at a meeting, of the Authority and shall be determined by the majority of the members present and voting.

(*b*) In the event of an equality of votes on any question considered at a meeting the Chairman of that meeting shall have a casting vote in addition to his original vote.

(*c*) All decisions of the Authority supported by reasons, shall be in writing and the seal of the Authority affixed thereto.

(3) (*a*) Any member of the Authority may by written notice, request the Chairman to call a meeting and the Chairman shall not otherwise than for justifiable reasons refuse to do so.

(*b*) The Chief Executive Officer appointed under section 15 shall summon all meetings of the Authority.

(4) No act, decision or proceeding of the Authority, shall be deemed to be invalidated by reason only of the existence of any vacancy of the Authority or any defect in the appointment of any member thereof.

(5) The quorum for any meeting of the Authority shall be seven.

(6) Subject to the preceding provisions of this section, the Authority may regulate the procedure with regard to the meetings of the Authority and the transaction of business at such meeting.

The Seal.

11. (1) The seal of the Authority shall be as determined by the Authority.

(2) The seal of the Authority -

(*a*) may be altered in such manner as may be determined by the Authority;

(*b*) shall be in the custody of such person or persons as the Authority may, determine;

(*c*) shall not be affixed to any instrument or document without the sanction of the Authority and except in the presence of two members of the Authority, both of whom shall sign the instrument or document in token of their presence.

(3) The Authority shall maintain a register of documents to which the seal of the Authority has been affixed.

Authority to invite experts to meetings.

12. (*a*) The Authority may invite experts on a relevant subject matter to meetings of the Authority for the purpose of obtaining their views for the effective discharge of the functions of the Authority.

(*b*) The Authority shall have the discretion of accepting or rejecting the views of the experts.

(*c*) The experts shall have no voting rights.

Remuneration for attending meetings of the Authority.

13. The members of the Authority and the experts may be paid such remuneration for attendance at meetings of the Authority, as may be determined by the Minister with the concurrence of the Minister assigned the subject of Finance.

Powers and functions of theAuthority.

14. The powers and functions of the Authority shall be to :-

(*a*) decide on classifying a product as a medicine, medical device, borderline product or any other product;

(*b*) authorize registration and licensing of medicines, medical devices, borderline products and investigational medicinal products or cancel or suspend any such registration or licence in terms of this Act;

(*c*) regulate the registration, licensing, manufacture, importation, storage, re-packing, transportation, distribution, sale, advertising, promotion, recall and disposal of medicines, medical devices, borderline products or investigational medicinal products;

(*d*) authorize registration and regulation of Pharmacies and medicines stores;

(*e*) issue licences for manufacture, import, storage, distribution, transport and sale of medicines, medical devices, borderline products or investigational medicinal products and to cancel such licences in terms of this Act;

(*f*) appoint sub-committees as may be necessary for the effective discharge of the functions of the Authority;

(*g*) grant approval for the custom clearance of consignments of medicines, medical devices, borderline products, raw materials, packing materials, machinery or laboratory material needed for local manufacture of medicines, medical devices, borderline products or investigational medicinal products subject to the provisions of this Act and any other written law;

(*h*) conduct awareness programmes in relation to medicines, medical devices and borderline products and post market surveillance on the quality and safety of medicines, medical devices, borderline products and investigational medicinal products which are registered and licensed under this Act;

(*i*) monitor the registration and licensing process and the usage of medicines, medical devices, borderline products or investigational medicinal products which are registered and licensed under this Act for adverse reactions through use thereof, and to take immediate and necessary action in such an instance;

(*j*) collect data on quantities of medicines, medical devices, borderline products or investigational medicinal products imported under licences;

(*k*) collect data on utilization of medicines, medical devices, borderline products and investigational medicinal products in Sri Lanka, including data on expenditure of industry and trade, relating to promotional activities;

(*l*) advise the Minister on matters which are required to be prescribed;

(*m*) acquire, hold, take or give on lease or hire, mortgage, pledge, sell or otherwise dispose of, any movable or immovable property;

(*n*) charge fees where necessary and appropriate in the discharge of its functions;

(*o*) recognize and appoint other local or overseas laboratories for testing of any medicine, medical device or borderline product as may be deemed necessary;

(*p*) follow Good Regulatory Practices (GRP) as prescribed in regulations;

(*q*) determine the initial price of medicines, medical devices and borderline products and advise the Minister on subsequent price revisions;

(*r*) provide information pertaining to the functions of the Authority to the stakeholders and general public; and

(*s*) issue, review and update guidelines, recommendations, directives and rules as applicable to medicines, medical devices and borderline products.

PART II

APPOINTMENT OF CHIEF EXECUTIVE OFFICER AND STAFF OF THE AUTHORITY

Appointment of the Chief Executive Officer of the Authority.

15. (1) The Authority shall in consultation with the Minister, appoint to the Staff of the Authority a Chief Executive Officer (hereinafter referred to as the "CEO") from among persons who hold a postgraduate degree from a recognized University in Medicine, Pharmacology, Pharmacy or any other related discipline with at least five years management experience at senior executive level.

(2) The CEO shall subject to the general directions and supervision of the Authority -

(*a*) be charged with the administration of the affairs of the Authority including the administration and control of the staff;

(*b*) be responsible for the execution of all decisions of the Authority;

(*c*) carry out all such functions as may be assigned to him by the Authority; and

(*d*) function as the Secretary to the Authority.

(3) The Authority may in consultation with the Minister remove the CEO from office -

(*a*) if he becomes permanently incapable of performing his duties;

(*b*) if he has done any act which, is of a fraudulent or illegal character or is prejudicial to the interests of the Authority; or

(*c*) has failed to comply with any directions issued by the Authority.

(4) The term of office of the CEO shall be for a period of three years from the date of appointment and shall be eligible for re-appointment.

(5) The office of the CEO shall become vacant upon the death, removal from office under subsection (3) or resignation by letter in that behalf addressed to the Minister by the holder of that office.

(6) If any vacancy occurs in the office of the CEO, the Authority may appoint any other suitable officer of the Authority to perform the duties of the CEO until an appointment is made under subsection (1).

Staff of the Authority.

16. (1) The Authority may appoint such technical and other officers and employees as may be necessary for the efficient discharge of its functions.

(2) The Authority may, in respect of the officers and employees appointed to the Authority under subsection (1)-

(*a*) exercise disciplinary control over or dismiss such officers and employees;

(*b*) fix the rates at which such officers and employees shall be remunerated in keeping with related guidelines of the Government;

(*c*) determine the terms and conditions of employment of such officers and employees; and

(*d*) establish a staff welfare and social security schemes for the benefit of such officers and employees and make contributions to any such schemes.

(3) The Authority may make rules in respect of all or any of the matters referred to in subsections (1) and (2).

(4) The Authority shall not however appoint as an officer or an employee of the Authority, any person who has been dismissed from any previous position held by such person in the public or private sector as an officer or an employee.

Public officers to be appointed to the Staff of the Authority.

17. (1) At the request of the Authority any officer in the public service may, with the consent of that officer and the Secretary to the Ministry under which that officer is employed, and the Secretary to the Ministry of the Minister assigned the subject of Public Administration, be temporarily appointed to the staff of the Authority for such period as may be determined by the Authority or with like consent, be permanently appointed to such staff.

(2) Where any officer in the public service is temporarily appointed to the staff of the Authority, the provisions of section 14(2) of the National Transport Commission Act, No.37 of 1991 shall, *mutatis mutandis*, apply to and in relation to such officer.

(3) Where any officer in the public service is permanently appointed to the staff of the Authority, the provisions of section 14(3) of the National Transport Commission Act, No.37 of 1991 shall, *mutatis mutandis*, apply to and in relation to such officer.

(4) Where any officer or employee of the Department of Health is appointed to the staff of the Authority, the provisions of sections 16, 17, 18 and 19 of the National Aquaculture Development Authority of Sri Lanka Act, No. 53 of 1998 shall *mutatis mutandis* apply to and in relation to such officer or employee.

(5) Where the Authority employs any person who has entered into a contract with the Government by which he

has agreed to serve the Government for a specified period, any period of service with the Authority by that person shall be regarded as service to the Government for the purpose of discharging the obligations of such contract.

PART III

FINANCE

Fund of the Authority.

18. (1) The Authority shall have its own Fund.

(2) There shall be paid into the Fund -

(*a*) all such sums of money as may be voted upon from time to time by Parliament for the use of the Authority;

(*b*) all such sums of money as may be received by the Authority by way of charges and levied for services provided by the Authority under this Act;

(*c*) all such sums of money as may be received by the Authority in the exercise, performance and discharge of its powers and functions under this Act;

(*d*) all such sums of money as may be received by the Authority by way of loans, donations, gifts and grants ;

(*e*) all such sums of money accruing to the credit of the Authority; and

(*f*) all such sums of money received by alienating, leasing or renting of property owned by the Authority.

(3) There shall be paid out of the Fund all such sums of money required to defray the expenditure incurred by the Authority in the exercise and performance of its powers and functions under this Act.

Authority to maintain accounts.

19. The Authority may open and maintain any account with any bank as it may think appropriate, and such account shall be operated in accordance with prevailing financial regulations of the Government pertaining to financial transactions of public corporations.

Financial year and audit of accounts.

20. (1) The financial year of the Authority shall be the calendar year.

(2) The Authority shall cause proper books of accounts to be kept of the income and expenditure, assets and liabilities and all other financial transactions of the Authority.

(3) For the purpose of presenting a true and fair view of the financial performance and financial condition of the Authority, the Authority shall prepare the accounts in accordance with the Sri Lanka Accounting Standards adopted by the Institute of Chartered Accountants of Sri Lanka under the Sri Lanka Accounting and Auditing Standards Act, No. 15 of 1995.

(4) The provisions of Article 154 of the Constitution relating to the audit of accounts of public corporations shall apply to the audit of the accounts of the Authority.

Investment of funds.

21. Moneys belonging to the Authority may, with the approval of the Minister and with the concurrence of the Minister assigned the subject of Finance, be invested in Government approved securities.

Borrowing powers of the Authority.

22. (1) The Authority may, with the written consent of the Minister and the Minister assigned the subject of Finance and in accordance with the terms of any general authority given, borrow or obtain on credit terms such sums as the Authority may require to meet the obligations of the Authority.

(2) The aggregate of the amount outstanding in respect of any loans raised by the Authority under this section shall not at any time exceed such amount as may be determined by the Minister.

PART IV

GENERAL

Annual Report.

23. (1) The Authority shall within six months of the end of each financial year, submit to the Minister an annual report of the activities carried on by the Authority during that financial year, and cause a copy each of the following documents to be attached to the report –

(*a*) the audited accounts of the Authority for the year along with the Auditor-General's report; and

(*b*) a report of proposed activities for the year immediately following, the year to which such report and accounts relates.

(2) The Minister shall lay copies of the report and documents submitted under subsection (1) before Parliament within six months from the date of receipt of such report.

Declaration of secrecy.

24. Every member of the Authority and all officers and employees of the Authority shall, before entering upon duties, sign a declaration pledging to observe strict secrecy in respect of all matters connected with the affairs of the Authority, which has come to his knowledge in the performance or exercise of his powers and functions under this Act and shall by such declaration pledge himself not to disclose any such matter, except -

(*a*) when required to do so by a court of law; or

(*b*) for the purpose of exercising or performing the powers and functions under this Act or any other written law.

Delegation of powers of the Authority.

25. (1) The Authority may in writing and subject to such conditions as may be specified therein, delegate to the CEO and any Head of the relevant division of the Authority any of its powers or functions and any such person or any Head of the relevant division shall exercise or perform such powers or functions in the name and on behalf, of the Authority.

(2) The Authority may, notwithstanding any delegation made under subsection (1), by itself exercise or perform any power or function so delegated and may at any time revoke any such delegation.

Directions by the Minister.

26. (1) The Minister may from time to time, issue to the Authority such general or special directions in writing as to the exercise and performance of its powers and functions so as to ensure the giving proper effect to Government Policy and it shall be the duty of the Authority to give effect to such directions.

(2) The Minister may direct the Authority to furnish to him in such form as he may require, returns, accounts and any other information relating to the work of the Authority, and it shall be the duty of the Authority to give effect to such directions.

Officers and employees of the Authority deemed to be public officers.

27. The CEO and the officers and employees of the Authority shall be deemed to be public officers within the meaning of and for the purposes of the Penal Code .

Authority deemed to be a Scheduled institution.

28. The Authority shall be deemed to be a Scheduled Institution within the meaning and for the purposes of the Bribery Act and the provisions of that Act shall be construed accordingly.

Expenses in suit or prosecution to be paid out of the Fund.

29. (1) Any expenses incurred by the Authority in any suit or prosecution brought by or against it before any Court, shall be paid out of the Fund of the Authority and any costs paid to or recovered by the Authority in any such suit or prosecution shall be credited to the Fund of the Authority.

(2) Expenses incurred by any member, the CEO or any officer or employee of the Authority in any suit or prosecution brought against him before any Court or Tribunal in respect of any act which is done or purported to be done by him under the provisions of this Act or any other written law or if the court holds that such act was done in good faith, be paid out of the Fund of the Authority, unless such expenses are recoverable by him in such suit or prosecution.

CHAPTER II

NATIONAL ADVISORY COMMITTEE AND DIVISIONS OF THE AUTHORITY

PART I

ESTABLISHMENT OF NATIONAL ADVISORY COMMITTEE AND DIVISIONS

Establishment of National Advisory Committee and divisions.

30. (1) There shall be established a National Advisory Committee, the main function of which shall be to advise the Minister and the Authority on matters pertaining to proper implementation of the National Medicines Policy of Sri Lanka.

(2) There shall be established divisions of the Authority including the following divisions-

(i) National Medicine Quality Assurance Laboratory (NMQAL) which shall be responsible for the analysing of the quality of any medicine, medical device or borderline product forwarded by the Authority.

(ii) Medicines Regulatory Division, which shall be responsible for regulation and control of all aspects pertaining to medicines as may be authorized and directed by the Authority;

(iii) Medical Devices Regulatory Division which shall be responsible for regulation and control of all aspects pertaining to medical devices as may be authorized and directed by the Authority;

(iv) Borderline Products Regulatory Division which shall be responsible for regulation and control of all aspects pertaining to borderline products as may be authorized and directed by the Authority;

(v) Clinical Trials Regulatory Division which shall be responsible for regulation and control of all aspects pertaining to clinical trials carried out in Sri Lanka as may be authorized and directed by the Authority;

(vi) Information, Education, Communication and Research Division which shall be responsible for educating the people as well as stake holders and healthcare professionals on rational use of medicines, medical devices and borderline products and promoting research into medicines, medical devices and borderline products as may be authorized and directed by the Authority;

(vii) Inspectorate and Enforcement Division which shall be responsible for inspecting and investigating issues pertaining to proper implementation of the provisions of this Act as may be authorized and directed by the Authority;

(viii) Pharmacovigilance Division which shall be responsible for monitoring and dealing with adverse drug reaction, quality failure and counterteit medicines as may be authorized and directed by the Authority;

(ix) Pharmacies Regulatory Division which shall be responsible for the regulation and control of pharmacies in Sri Lanka as may be authorized and directed by the Authority;

(x) Manufacturing Regulatory Division which shall be responsible for the regulation and promotion of manufacturing of good quality medicines, medical devices and borderline products in Sri Lanka; and

(xi) Organization Development Division which shall be responsible for the Human Resources, Finance, Administration and Audit of the Authority as may be authorized and directed by the Authority.

(3) The Authority shall appoint a head to each division who shall communicate with the Authority on behalf of such division.

(4) The Authority may where necessary-

(*a*) establish any other division or sub division;

(*b*) merge any two or more divisions or discontinue any division or subdivision.

(5) The Authority shall appoint such number of officers, employees and advisors as may be necessary for the proper discharge of the functions of a division or a sub division.

(6) All rules and regulations applicable for the Staff of the Authority referred to in sections 16 and 17 of this Act shall be applicable to the officers, advisors and employees of any division or sub division.

PART II

NATIONAL ADVISORY COMMITTEE

Constitution of the National Advisory Committee.

31. (1) The National Advisory Committee shall consist of the following members appointed by the Minister -

(*a*) the Director General of Health Services;

(*b*) the Deputy Director General of Health Services (Laboratory Services);

(*c*) the Chairman of the Authority;

(*d*) a nominee from the Secretary to the Treasury;

(*e*) the Chairman of the State Pharmaceuticals Corporation of Sri Lanka established under State Industrial Corporation Act, No. 49 of 1957;

(*f*) a Professor in Pharmacology in any University in Sri Lanka established under the Universities Act, No. 16 of 1978, appointed in consultation with the respective Deans of the relevant Medical Faculties;

(*g*) a Pharmacologist from the Ministry of Health nominated by the Director General of Health Services;

(*h*) the President of the Sri Lanka Medical Association or his nominee;

(*i*) the President of the Pharmaceutical Society of Sri Lanka or his nominee;

(*j*) the Commissioner of Ayurveda or his nominee;

(*k*) Director General of Customs or his nominee;

(*l*) a legal officer from the Ministry of Health nominated by the Secretary;

(*m*) a representative of the Ceylon College of Physicians nominated by that College;

(*n*) a representative of the College of Surgeons of Sri Lanka nominated by that College;

(*o*) a representative of the College of General Practitioners of Sri Lanka nominated by that College;

(*p*) a representative of the College of Community Physicians of Sri Lanka nominated by that College;

(*q*) a representative from the Attorney General's Department nominated by the Attorney General;

(*r*) a representative from the Consumer Affairs Authority nominated by the Chairman of that Authority;

(*s*) a representative of the Sri Lanka Standards Institution established under the Sri Lanka Standards Institution Act, No. 6 of 1984, nominated by the Director General of such Institution;

(*t*) a representative from a patient interest group nominated by the Minister of Health;

(*u*) a representative from the Sri Lanka Pharmaceutical Manufacturers Association nominated by that Association;

(*v*) a representative from the Sri Lanka Chamber of the Pharmaceutical Industry nominated by such Chamber;

(*w*) a representative of the public nominated by the Minister; and

(*x*) a representative of the Senaka Bibile Commemoration Committee.

(2) (*a*) Every member of the National Advisory Committee nominated under paragraphs (*m*), (*n*), (*o*), (*p*), (*q*), (*r*), (*s*), (*t*),(*u*),(*v*), (*w*) and (*x*) of subsection (1) shall, unless earlier vacates office by resignation, death or removal, hold office

for a period of three years from the date of appointment and shall be eligible for re-appointment.

(*b*) Every other member of the National Advisory Committee shall hold office so long as such member holds office by virtue of which such member has been appointed to the National Advisory Committee.

Chairman &c., of the National Advisory Committee.

32. (1) The Minister shall appoint any member of the National Advisory Committee as the Chairman of the National Advisory Committee.

(2) The National Advisory Committee may discharge its functions notwithstanding any vacancy among its membership.

(3) The quorum for any meeting of the National Advisory Committee shall be eleven members.

(4) Subject to the provisions of this Act, the National Advisory Committee may regulate its own procedure in regard to its meetings and transactions of business at such meetings.

Remuneration of the members of the National Advisory Committee.

33. The members of the National Advisory Committee, shall not receive any remuneration for being in the National Advisory Committee, except an honorarium which may be given for attending at the meetings of the National Advisory Committee.

Appointment of officers, employees &c.

34. (*a*) The Authority shall appoint such number of officers employees and advisors as may be necessary for the proper discharge of the functions of the National Advisory Committee.

(*b*) All rules and regulations applicable for the staff of the Authority referred to in sections 16 and 17 of this Act shall be applicable to the officers, employees and advisers referred to paragraph (*a*).

Functions of the National Advisory Committee.

35. The functions of the National Advisory Committee shall be -

(*a*) the overall supervision of the proper implementation of the provisions of this Act;

(*b*) the overall supervision of the proper implementation of the national medicines policy; and

(*c*) to advise the Minister and the Authority on issues pertaining to the matters specified in paragraphs (*a*) and (*b*) and any other related matters.

Regulations.

36. The Minister may make regulations to give effect to the provisions of this Part of this Act.

Application of certain provisions of this Act in relation to National Advisory Committee.

37. The provisions of sections 5, 6, 7, 8, 9, 10, 11, 12 and 13 of this Act shall *mutatis mutandis* apply to and in relation to the Chairman, members and the conducting of the affairs of the National Advisory Committee.

PART III

NATIONAL MEDICINES QUALITY ASSURANCE LABORATORY

Establishment of the National Medicines Quality Assurance Laboratory.

38. (1) For the purpose of this Act there shall be a Division to be known as the National Medicines Quality Assurance Laboratory (hereinafter referred to as the "NMQAL").

(2) (*a*) The National Drug Quality Assurance Laboratory functioning under the Ministry of the Minister on the day immediately preceding the appointed date shall, with effect from the appointed date, be vested with the Authority and shall be deemed to be the NMQAL for the purposes of this Act.

(*b*) All testing assignments and other work assigned to the National Drug Quality Assurance Laboratory and pending on the appointed date, shall, with effect from the appointed date, be carried out and completed by the NMQAL.

(*c*) Any officer or employee of the National Drug Quality Assurance Laboratory may, with effect from the appointed date, be employed in the NMQAL and the provisions of sections 16, 17, 18 and 19 of the National Aquaculture Development Authority of Sri Lanka Act, No. 53 of 1998 shall *mutatis mutandis* apply to and in relation to such officer or employee.

Functions of NMQAL.

39. (1) The functions of the NMQAL shall be -

(*a*) the testing of the quality of medicines, medical devices or borderline products submitted by the Authority including the articles -

(i) submitted with the application for registration;

(ii) collected at the entry to the country;

(iii) submitted as a complaint by users;

(iv) collected during the post marketing surveillance by the Authority;

(v) submitted by the Authority for any reason other than the reasons specified above;

(*b*) to function, as an additional approved Analyst, when the circumstances so require;

(*c*) to coordinate with laboratories local or overseas when their services are deemed necessary as decided by the Authority;

(*d*) to carry out research projects pertaining to quality assurance of medicines, medical devices or borderline products.

(2) The NMQAL shall carry out any other functions as may be requested by the Authority and the Department of Health through the Authority.

(3) The NMQAL shall carry out any testing or analysis of an article submitted to the NMQAL strictly according to the quality and standards guidelines as may be introduced by the Authority, from time to time.

(4) The NMQAL shall submit the analysis report on the quality and standards of the article submitted within the time period stipulated by the Authority.

(5) For the purposes of this part of this Act "article" includes any article of medicine, medical device, borderline product or investigational medicinal product.

Regulations.

40. The Minister may make regulations to give effect to the provisions of this Part of this Act.

CHAPTER III

REGULATION AND CONTROL OF ALL ASPECTS PERTAINING TO MEDICINES

PART I

MEDICINES REGULATORY DIVISION

Medicines Regulatory Division.

41. (1) The Medicines Regulatory Division established under section 30(2) shall hereinafter in this Act be referred to as the MR Division.

(2) The Authority shall appoint the head of the MR Division from among persons holding a recognized degree in Medicine, Pharmacology, Pharmacy or any other related discipline.

Functions of the MR Division.

42. (*a*) The principal function of the MR Division shall be to co-ordinate and assist the Authority to regulate and control all aspects pertaining to medicines.

(*b*) The other functions of the MR Division shall be the -

(i) co-ordination of applications submitted for registration of medicines and renewal of such registration;

(ii) co-ordination of matters pertaining to cancellation or suspension of registration of medicines;

(iii) co-ordination of matters pertaining to registration of importers and distributers of medicines;

(iv) co-ordination of the issuance of licences under this section; and

(v) provisions of administrative assistance to the Medicines Evaluation Committee appointed under section 43 of this Act.

PART II

MEDICINES EVALUATION

Medicines Evaluation Committee.

43. (1) There shall be appointed for the purposes of this Act, a Committee which shall be known as the Medicines Evaluation Committee (hereinafter referred to as "the MEC").

(2) (*a*)The principal function of the MEC shall be to carry out the technical evaluation of the medicines forwarded for registration and submit a report in respect thereof to the Authority.

(*b*) The report shall specify the benefits and risks attached to such medicines and the quality, efficacy, safety, need and cost of such medicines with pharmacoeconomic analysis where necessary in keeping with the National Medicines Policy.

Constitution of the MEC.

44. (1) The MEC shall consist of the following persons who shall be appointed by the Authority -

(a) *ex officio* members –

(i) the head of the MR Division who shall function as the Chairman of the Committee;

(ii) the head of the National Medicines Quality Assurance Laboratory (NMQAL);

(*b*) nominated members -

(i) four specialist clinicians attached to the Ministry of Health representing the following fields, nominated by their respective professional bodies-

(A) General Medicine;

(B) General Surgery;

(C) Pediatrics; and

(D) Gynaecology and Obstetrics;

(ii) a Professor in Pharmacology in University of Colombo established under the Universities Act, No. 16 of 1978, nominated by the Dean of the Faculty of Medicine;

(iii) a Professor or Senior Lecturer in Pharmacy of any University established under the Universities Act, No.16 of 1978, nominated by the Deans of relevant Faculties; and

(iv) a Pharmacist functioning under the Authority.

(2) The quorum for meetings shall be five members excluding the members of the Panel of Experts.

(3) The term of office of a nominated member shall be three years.

Panel of Experts.

45. (1) The Authority shall appoint a Panel of Experts, comprising of eminent professionals of medicine and other relevant fields.

(2) The Authority may where necessary appoint additional members to the MEC from the Panel of Experts, depending on the subject matter dealt with by the MEC.

(3) The members appointed under subsection (2) shall be present at the meetings for which their presence is required and express their opinion but they shall have no voting rights at such meetings.

Declaration of secrecy.

46. Every member of the MR Division and the MEC and all officers and employees of the MR Division and the MEC shall, before entering upon duties, sign a declaration pledging to observe strict secrecy in respect of all matters connected with the affairs of the MR Division and the MEC, which has come to his knowledge in the performance or exercise of his powers and functions under this Act and shall by such declaration pledge himself not to disclose any such matter, except -

(*a*) when required to do so by a court of law; or

(*b*) for the purpose of exercising or performing the powers and functions under this Act or any other written law.

Authority to give general guidelines for the evaluation.

47. (1) The Authority shall issue general guidelines to the MEC for the evaluation of medicines and other related items, submitted to the MEC.

(2) (*a*) The general guide lines referred to in subsection (1) shall be based on the Good Manufacturing Practices (GMP) and other recommendations issued by the World Health Organization and other regulatory bodies recognized by the Authority.

(*b*) The Authority may revise the general guidelines from time to time in order to maintain parallels with internationally recognized standards and practices.

(3) The MEC shall take into consideration the efficacy, safety, quality, need and cost of each medicine, in the process of evaluation and may consider pharmacoeconomic analysis where necessary.

(4) The Minister may make regulations -

(*a*) setting out the procedures to be followed, including the specified time limits, for the conduct of respective evaluations;

(*b*) to give effect to the Good Manufacturing Practices (GMP) guidelines, Good Review Practices (GRP) and any other applicable guidelines as may be recommended by the Authority; and

(*c*) in respect of bioequivalence and biowaiver data relating to generic medicines submitted for evaluation.

Application of certain provisions of this Act in relation to MEC.

48. The provisions of sections 5, 6, 7, 8, 9, 10, 11, 12 and 13 of this Act shall *mutatis mutandis* apply to and in respect of the Chairman, members and the conducting of the affairs of the MEC.

PART III

OFFENCES PERTAINING TO MEDICINE

Regulation of manufacture, importation, sale and distribution of medicine.

49. (1) No person shall import, distribute, exhibit or sell any medicine that-

(*a*) is manufactured, prepared, preserved, packaged or stored under insanitary conditions;

(*b*) consists in whole or in part any contaminant or decomposed substance or any foreign matter;

(*c*) has in or upon it any deleterious substance that may cause injury to the health of the user; or

(*d*) is adulterated.

(2) No person shall manufacture, prepare, store, preserve, package or re-pack any medicine without adhering to Good Manufacturing Practices (GMP) and any other prescribed guidelines or conditions.

(3) No person shall import or distribute any medicine without adhering to Good Distribution Practices (GDP) and any other prescribed guidelines and conditions.

Labelling, &c.,to be in conformity with the prescribed standards.

50. (1) Where the standard is prescribed for any medicine, no person shall label, package, sell, exhibit, distribute or advertise any medicine which does not conform to such standard or in such manner as is likely to be mistaken for the medicine for which the standard has been prescribed.

(2) Where the standard has not been prescribed for any medicine, but a standard for that medicine is contained in any prescribed publication, no person shall label, package, sell, exhibit, distribute or advertise any medicine which does not conform to the standard contained in that publication in such a manner as is likely to be mistaken for the medicine which the standard is contained in that publication.

(3) Where a standard has not been prescribed for any medicine, or a standard for that medicine is not contained in any prescribed publication, no person shall sell, exhibit or distribute such medicine –

(*a*) unless it is in conformity with the standard set out in the label accompanying the medicine; or

(*b*) in such a manner as is likely to be mistaken for a medicine for which a standard has been prescribed or for which a standard is contained in any prescribed publication.

(4) No person shall label, package, re-pack, treat, process, sell, distribute, exhibit or advertise any medicine in a manner that is false, misleading, deceptive or likely to create an erroneous impression regarding efficacy, quality, composition or safety.

(5) A medicine that is not labeled or packaged in a manner as may be prescribed shall be deemed to be labeled or packaged contrary to subsection (1).

Sale of prescribed medicine is prohibited unless premises and process of manufacture have been approved.

51. No person shall sell, exhibit or distribute any medicine as may be prescribed unless the premises in which the medicine was manufactured and the process and conditions of manufacture of that medicine have been approved in the prescribed form and manner as being suitable to ensure that the medicine will be safe for use.

Sale of prescribed medicine prohibited unless the batch from which such medicine is taken approved as reliable.

52. No person shall sell, exhibit or distribute any medicine as may be prescribed unless the batch from which that medicine was taken has been approved in the prescribed form and manner as reliable for use.

Sale &c., of prohibited medicine.

53. No person shall manufacture, import, store, sell, re-pack, distribute, transport, exhibit or have in his possession any medicine which is prescribed as not safe for use.

Possession of prohibited medicine.

54. No person other than the persons as may be permitted by regulations shall obtain or have in his possession any medicine restricted or prohibited by regulations.

Advertising, importation, sale and distribution of medicine as treatment for prescribed diseases prohibited.

55. (1) No person shall advertise or promote any medicine without prior written approval of the Authority.

(2) No person shall advertise or promote any medicine to the general public as a treatment, prevention or cure for any of the prescribed diseases, disorders or abnormal physical states.

(3) No person shall, without prior written approval of the Authority, import, sell or distribute any medicine to the general public as a treatment, prevention or cure for any of the prescribed diseases, disorders or abnormal physical states.

Generic name of a medicine to be written in the prescription.

56. (1) Every Medical Practitioner, Dentist or Veterinary Surgeon shall write the generic name of the medicine in every prescription issued by him.

(2) Where the Medical Practitioner, Dentist or Veterinary Surgeon so requires, he may in addition to the generic name write a particular brand name of the medicine in the prescription.

(3) A Medical Practitioner, Dentist or Veterinary Surgeon may write only the brand name of a medicine in the prescription where the medicine prescribed is a combined medicine for which the generic name is not available.

(4) Where the brand name of the medicines, which is in the prescription is not available or affordable to the customer, the Pharmacist may dispense any other generic medicine with the consent of the customer.

(5) The Pharmacist shall inform the customer the range of generic medicines with or without brand names available in the Pharmacy and their prices enabling the customer to buy the medicine according to his choice.

(6) A Pharmacist who fails to disclose the generic medicines with or without brand names available in the Pharmacy and their prices to the customer at the time of sale, commits an offence.

Contravention of the provisions of this Part to be an offence.

57. Any person who contravenes any of the provisions specified in this Part of this Act commits an offence.

PART IV

REGISTRATION AND LICENSING OF MEDICINES

Requirement to register &c., of medicines.

58. (1) No person shall manufacture or import any medicine without registering such medicine with the Authority and obtaining a licence from the Authority therefor.

(2) No person shall store, assemble, re-pack, distribute, transport or sell any medicine without obtaining a licence for that purpose from the Authority.

(3) Any person who contravenes any of the provisions specified in subsection (1) or (2) commits an offence.

Application for Registration of a medicine.

59. (1) Any person who intends to manufacture or import any medicine shall make an application for the registration of that medicine in the prescribed form to the Authority.

(2) The application shall be accompanied by the prescribed particulars, the samples of the medicine and the prescribed fee.

(3) (*a*) The Authority shall maintain a register in which every application received for the registration of a medicine shall be recorded.

(*b*) The particulars to be entered in such register shall be as prescribed.

(4) The Authority shall upon receipt of an application submit that application together with the sample of the medicine and all particulars, available -

(*a*) to the MEC, for the evaluation of the application and the medicine considering the need to ensure the availability of efficacious, safe and good quality medicine relevant to the healthcare needs of the public at an affordable price; and

(*b*) to the NMQAL, for testing of the quality of the medicine.

(5) The Authority shall inform the applicant in writing that the application has been received and submitted for evaluation and testing.

(6) The Minister may make regulations -

(*a*) setting out the procedures to be followed, by the MEC and the NMQAL in their respective evaluation and testing processes;

(*b*) specifying –

(i) the time-limits in conducting such testing or evaluation;

(ii) the manner in which the MEC to conduct its meetings and the procedure to be followed at such meetings; and

(iii) the matters which should be included in the reports to be submitted.

(7) (*a*) The Authority may require the MEC and the NMQAL to finalize the evaluation or testing of a medicine within a specified time period considering the urgency of such medicine for the national health.

(*b*) The MEC and the NMQAL shall within the time limits specified submit their reports to the Authority unless there are compelling reasons for any delay.

Registration of medicines.

60. (1) (*a*) The Authority may where necessary, call for clarifications from the MEC, NMQAL or any other expert, with regard to the reports submitted by the MEC and the NMQAL.

(*b*) The Authority may upon taking into consideration the reports submitted by the MEC, NMQAL and all other relevant factors, register such medicine, or refuse the registration, within the stipulated time period.

(2) Where the Authority registers the medicine, such registration shall be informed to the applicant in writing and may inform the public of such registration by order published in the *Gazette.*

Refusal of Registration.

61. Where the Authority refuses the registration of the medicine, such refusal shall be communicated to the applicant with reasons therefor within the stipulated time period and shall inform the public of such refusal by order published in the *Gazette*.

Issuing of certificate of registration.

62. (1) (*a*) The Authority shall on registration of any medicine, issue a Certificate of Registration to the applicant who shall, hereinafter in this part of this Act, be referred to as "the holder of certificate".

(*b*) The Authority may grant full or provisional registration in respect of the medicine and the conditions for each type of registration shall be prescribed.

(*c*) The period of registration granted shall be decided by the Authority as appropriate.

(2) The Certificate of Registration shall include the purpose for which the registration is granted, its period of validity and the terms and conditions applicable thereto.

(3) Upon obtaining the Certificate of Registration, the holder of certificate shall enter into an agreement with the Authority to inform the Authority of any new developments of the medicine including the changes to indications, side effects, cautions, contra-indications, new recommendations by regulatory bodies in other countries, strictures, cancellations within a stipulated time period upon such facts and information being revealed.

Issuing of licence.

63. (1) The Authority may upon issuing the Certificate of Registration, and on the written request by the holder of certificate, issue him a licence to import the medicine and market the medicine in Sri Lanka.

(2) It shall be the responsibility of the importer to ensure quality, safety and efficacy of every medicine imported by him.

Renewal.

64. (1) The holder of certificate may make an application to the Authority, for renewal of such registration or the licence six months prior to the date of expiry of such registration or the licence.

(2) The application for renewal of registration or the licence shall be in the prescribed form and shall be accompanied by the prescribed fee.

(3) The Authority shall, upon receiving an application, submit the application to the MEC for its opinion.

(4) The MEC may, through the Authority, request for samples, documents or any other evidence, which it deems necessary, from the applicant or any other person or institution for the evaluation of the medicine.

(5) The MEC may, where the MEC deems necessary, request the NMQAL to submit an evaluation report on the medicine and the NMQAL shall submit the evaluation report as required by the MEC.

(6) The Authority may upon taking into consideration all relevant factors, renew the registration or the licence for a further period of not less than one year and not exceeding five years.

Cancellation or suspension of registration and licence.

65. (1) Where the Authority is of the opinion that –

(*a*) the holder of certificate has failed to comply with any condition subject to which any medicine has been registered;

(*b*) the medicine does not comply with any prescribed requirement;

(*c*) it is not in the public interest that the medicine shall be available;

(*d*) the medicine has not been imported to Sri Lanka within two years from the date of registration;

(*e*) the holder of certificate has failed to comply with any direction of the Authority; or

(*f*) the holder of certificate has violated any provision of this Act or any regulation made thereunder,

the Authority shall cause notice of cancellation or suspension to be issued to the holder of certificate in respect of such medicine.

(2) Any such notice shall specify the grounds on which the Authority's opinion is based, and shall indicate that the holder of certificate may within one month after receipt thereof submit to the Authority in writing any comments he may wish to submit.

(3) Where the holder of certificate fails to submit his comments within the time stipulated therefor or after consideration of any comments submitted, the Authority may suspend or cancel the Certificate of Registration and any related license and inform in writing the suspension or cancellation to the holder of certificate immediately.

(4) Where the holder of certificate, does not apply for a renewal of such Certificate six months before its expiry date, the registration or licence of the medicine for which such Certificate relates, shall be deemed to have automatically been cancelled.

CHAPTER IV

REGULATION AND CONTROL OF ALL ASPECTS PERTAINING TO MEDICAL DEVICES

PART I

MEDICAL DEVICES REGULATORY DIVISION

Medical Devices Regulatory Division.

66. (1) The Medical Devices Regulatory Division established under section 30(2) shall hereinafter in this Act be referred to as the MDR Division.

(2) The Authority shall appoint the head of the MDR Division from among persons holding a recognized degree in Medicine, Pharmacology, Pharmacy or any other related discipline.

Functions of the MDR Division.

67. (*a*) The principal function of the MDR Division shall be to co-ordinate and assist the Authority to regulate and control all aspects pertaining to medical devices.

(*b*) The other functions of the MDR Division shall be the -

(i) co-ordination of applications submitted for registration of medical devices and renewal of such registration;

(ii) co-ordination of matters pertaining to cancellation or suspension of registration of medical devices;

(iii) co-ordination of matters pertaining to registration of importers and distributers of medical devices;

(iv) co-ordination of the issuance of licences under this section; and

(v) provisions of administrative assistance to the Medical Devices Evaluation Committee appointed under section 68 of this Act.

PART II

MEDICAL DEVICES EVALUATION

Medical Devices Evaluation Committee.

68. (1) There shall be appointed for the purposes of this Act a Committee which shall be known as the Medical Devices Evaluation Committee (hereinafter referred to as "the MDEC").

(2) (*a*) The principal function of the MDEC shall be to carry out the technical evaluation of the medical devices forwarded for registration and to submit a report in respect thereof to the Authority.

(*b*) The report shall specify the benefits, risks attached to such medical devices, and the efficacy, quality, safety, need and cost of such medical devices with pharmacoeconomic analysis where necessary in keeping with the National Medicines Policy.

Constitution of the MDEC.

69. (1) The MDEC shall consist of the following persons who shall be appointed by the Authority-

(*a*) *ex-officio* members-

(i) the head of the MDR Division who shall function as the Chairman of the Committee;

(ii) the Deputy Director General of Laboratory Services of the Ministry;

(iii) the Deputy Director - General of Dental Services of the Ministry;

(iv) the Deputy Director - General (Biomedical Engineering) of the Ministry;

(v) the Head of the National Medicines Quality Assurance Laboratory (NMQAL);

(*b*) nominated members-

(i) a Professor or a Senior Lecturer in Pharmacology of any University established under the Universities Act, No. 16 of 1978, nominated by the Deans of Medical Faculties of such Universities;

(ii) a Professor or Senior Lecturer in Pharmacy of any University in Sri Lanka established under the Universities Act, No.16 of 1978, nominated by the Deans of relevant Faculties;

(iii) a Professor or a Senior Lecturer in Biomedical Engineering from any University in Sri Lanka established under the Universities Act, No. 16 of 1978, nominated by the University Grants Commission;

(iv) the Director of the Sri Lanka Standards Institute established under the Sri Lanka Standards Institute Act, No.6 of 1984, or his nominee;

(v) the Director – General of the Sri Lanka Atomic Energy Board and the Director-General of the Sri Lanka Atomic Energy Regulatory Council appointed under the Sri Lanka Atomic Energy Act, No. 40 of 2014, or their nominees;

(vi) a Consultant in Transfusion Medicine, nominated by the Sri Lanka College of Transfusion Physicians;

(vii) a Consultant General Surgeon, nominated by the College of Surgeons of Sri Lanka;

(viii) a Consultant Microbiologist nominated by the Sri Lanka College of Microbiologists;

(ix) a Consultant Biochemist, nominated by the Association of Biochemists;

(x) a Consultant Anesthesiologist, nominated by the Sri Lanka College of Anesthesiologists;

(xi) an Oral Maxillo Facial Surgeon, nominated by the College of Dental Surgeons of Sri Lanka;

(xii) a Consultant Physician nominated by the Ceylon College of Physicians;

(xiii) a Consultant Radiologist nominated by the Sri Lanka College of Radiology; and

(xiv) a Pharmacist in charge of the subject of medical devices in the Authority nominated by the Authority.

(2) The quorum for meetings shall be seven members excluding the members of the Panel of Experts.

(3) The term of office of a nominated member shall be three years.

Panel of Experts.

70. (1) The Authority shall appoint a Panel of Experts, comprising of eminent professionals specialized in medical devices.

(2) The Authority may where necessary appoint additional members to the MDEC from the panel of experts, depending on the subject matter dealt with by the MDEC.

(3) The members appointed under subsection (2) shall be present at the meetings for which their presence is required and express their opinion but they shall have no voting rights at such meetings.

Declaration of secrecy.

71. Every member of the MDR Division and the MDEC and all officers and employees of the MDR Division and the MDEC shall, before entering upon duties, sign a declaration pledging to observe strict secrecy in respect of all matters connected with the affairs of the MDR division and the

MDEC, which has come to his knowledge in the performance or exercise of his powers and functions under this Act and shall by such declaration pledge himself not to disclose any such matter, except -

(*a*) when required to do so by a court of law; or

(*b*) for the purpose of exercising or performing the powers and functions under this Act or any other written law.

Authority to give general guidelines for the evaluation.

72. (1) The Authority shall issue general guidelines to the MDEC for the evaluation of medical devices and other related items, submitted to the MDEC.

(2) (*a*) The general guidelines referred to in subsection (1) shall be based on the Good Manufacturing Practices (GMP) guidelines and other recommendations and guidelines issued or recommended by the Authority.

(*b*) The Authority may revise the general guidelines from time to time in order to maintain parallels with internationally recognized standards and practices.

(3) The MDEC shall take into consideration the efficacy, safety, quality, need and cost of each medical device or related item in the process of evaluation and may consider pharmacoeconomic evaluation where necessary.

(4) The Minister may make regulations -

(*a*) setting out the procedures to be followed, including the specified time limits, for the conduct of respective evaluations;

(*b*) to give effect to the Good Manufacturing Practices (GMP) guidelines and any other applicable guide lines as may be recommended by the Authority;

Application of certain provisions of this Act in relation to MDEC.

73. The provisions of sections 5, 6, 7, 8, 9, 10, 11, 12 and 13 of this Act shall *mutatis mutandis* apply to and in relation to the Chairman, members and the conducting of the affairs of the MDEC.

PART III

OFFENCES PERTAINING TO THE MEDICAL DEVICES

Prohibition of importation &c., of medical devices other than the listed.

74. (1) The Authority shall list from time to time the medical devices registered under this Act.

(2) No person shall import, sell, transport, distribute or advertise any medical device, other than a medical device listed under subsection (1).

Regulation of manufacture, importation, sale and distribution of medical devices.

75. (1) No person shall manufacture, prepare, store, preserve, package or re-pack any medical device without adhering to Good Manufacturing Practices (GMP) and any other prescribed guidelines or conditions.

(2) No person shall import or distribute any medical device without adhering to Good Distribution Practices (GDP) and any other prescribed guidelines or conditions.

(3) No person shall sell any medical device without adhering to Good Pharmacy Practices and any other prescribed guideline or condition.

Prohibition of manufacturing, importation, assembling, sale and distribution &c., of medical devices.

76. No person shall manufacture, import, assemble, transport, sell or distribute any medical device that may cause any injury to the health of the user when that medical device is used—

(*a*) under conditions that are customary or usual in the use of the medical device; or

(*b*) according to the directions on the label accompanying that medical device.

Labeling, packaging and advertising of medical device.

77. No person shall label, package, treat, process, sell, assemble, distribute or advertise any medical device in a manner that is false, misleading, deceptive or likely to create an erroneous impression regarding its safety and efficacy.

Prescribed standards of a medical device to be maintained.

78. Where a standard is prescribed for any medical device, no person shall label, package, sell, distribute or advertise any medical device which does not conform to that standard or in such a manner as is likely to be mistaken for the medical device for which the standard has been prescribed.

Advertising, importation, sale and distribution of medical devices as a treatment for prescribed diseases prohibited.

79. (1) No person shall advertise or promote any medical device without prior written approval of the Authority.

(2) No person shall advertise or promote any medical device to the general public as a treatment, prevention or cure for any of the prescribed diseases, disorders or abnormal physical states.

(3) No person shall without prior written approval of the Authority import, sell or distribute any medical device to the general public as a treatment, prevention or cure for any of the prescribed diseases, disorders or abnormal physical states.

Possession of prohibited medical devices.

80. No person other than the persons as may be permitted by regulations shall obtain or have in his possession any medical device as may be restricted or prohibited by regulations.

Contravention of the provisions of this Part to be an offence.

81. Any person who contravenes any of the provisions specified in this Part of this Act commits an offence.

PART IV

Registration and Licensing of Medical Devices

Requirement to register &c., of medical devices.

82. (1) No person shall manufacture or import any medical device without registering such medical device with the Authority and obtaining a licence from the Authority therefor.

(2) No person shall store, assemble, re-pack, distribute, transport or sell any medical device without obtaining a licence for that purpose from the Authority.

(3) Any person who contravenes any of the provisions specified in subsection (1) or (2) commits an offence.

Application for Registration of a Medical device.

83. (1) Any person who intends to manufacture or import any medical device shall make an application for the registration of that medical device in the prescribed form to the Authority.

(2) The application shall be accompanied by the prescribed particulars, the samples of the medical device and the prescribed fee.

(3) (*a*) The Authority shall maintain a register in which every application received for the registration and licensing of a medical device shall be recorded.

(*b*) The particulars to be entered in such register shall be as prescribed.

(4) The Authority shall upon receipt of an application submit a copy of that application together with the sample of the medical device and all particulars, available –

(*a*) to the MDEC, for the evaluation of the application and the medical device considering the need to ensure the availability of efficacious, safe and good quality medical device relevant to the healthcare needs of the public at an affordable price; and

(*b*) to the NMQAL, for testing of the quality of the medical device.

(5) The Authority shall inform the applicant in writing of the receipt of the application.

(6) The Minister may make regulations –

(*a*) setting out the procedures to be followed, by the MDEC and the NMQAL in their respective testing or evaluation processes;

(*b*) specifying—

(i) the time-limits in conducting such testing or evaluation;

(ii) the manner in which the MDEC to conduct its meetings and the procedure to be followed at such meetings; and

(iii) the matters which should be included in the reports to be submitted.

(7) (*a*) The Authority may require the MDEC and the NMQAL to finalize the evaluation or testing within a specified time period considering the urgency of the medical device.

(*b*) The MDEC and the NMQAL shall within the time limits specified submit their reports to the Authority unless there are compelling reasons for any delay.

Registration of medical devices.

84. (1) (*a*) The Authority may where necessary, call for clarifications from the MDEC, NMQAL or any other expert, with regard to the reports submitted by the MDEC and the NMQAL.

(*b*) The Authority may upon taking into consideration the reports submitted by the MDEC, NMQAL and all other relevant factors register such medical device, or refuse the registration, within the stipulated time period.

(2) Where the Authority registers the medical device, such registration shall be informed to the applicant in writing and may inform the public of such registration by order published in the *Gazette.*

Refusal of Registration.

85. Where the Authority refuses the registration of the medical device, such refusal shall be informed to the applicant with reasons therefor within the stipulated time period and shall inform the public of such refusal by Order published in the *Gazette*.

Application of the provisions of sections 62, 63, 64 and 65.

86. The provisions of sections 62, 63, 64 and 65 of this Act shall *mutatis mutandis* apply to and in relation to—

(*a*) the issuing of certificate of registration;

(*b*) issuing of licence;

(*c*) renewal of registration or licence;

(*d*) cancellation or suspension of registration or licence,

under this part of this Act.

CHAPTER V

REGULATION AND CONTROL OF ALL ASPECTS PERTAINING TO BORDERLINE PRODUCTS

PART I

BORDERLINE PRODUCTS REGULATORY DIVISION

Borderline Products Regulatory Division.

87. (1) The Borderline Products Regulatory Division established under section 30(2) shall hereinafter in this Act be referred to as the BPR Division.

(2) The Authority shall appoint the head of the BPR division from among persons holding a recognized degree in Medicine, Pharmacology, Pharmacy or any other related discipline.

Functions of the BPR Division.

88. (*a*) The principal function of the BPR division shall be to co-ordinate and assist the Authority to regulate and control all aspects pertaining to borderline products.

(*b*) The other functions of the BPR division shall be the—

(i) co-ordination of applications submitted for registration of borderline products and renewal of such registration;

(ii) co-ordination of matters pertaining to cancellation or suspension of registration of borderline products;

(iii) co-ordination of matters pertaining to registration of importers and distributers of borderline products;

(iv) co-ordination of the issuance of licences under this section;

(v) provisions of administrative assistance to the Borderline Products Evaluation Committee appointed under section 89 of this Act.

PART II

BORDERLINE PRODUCTS EVALUATION

Borderline Products Evaluation Committee.

89. (1) There shall be appointed for the purposes of this Act a Committee which shall be known as the Borderline Products Evaluation Committee (hereinafter referred to as "the BPEC").

(2) (*a*) The principal function of the BPEC shall be to carry out the technical evaluation of the borderline products forwarded for registration and submit a report in respect thereof to the Authority.

(*b*) The report shall specify the benefits, risks attached to such borderline products, and the efficacy, quality, safety, need and cost of such borderline products with pharmacoeconomic analysis where necessary in keeping with the National Medicines Policy.

Constitution of the BPEC.

90. (1) The BPEC shall consist of the following persons who shall be appointed by the Authority—

(*a*) ex-officio members—

(i) the head of the BPR Division who shall function as the Chairman of the Committee;

(ii) the head of the National Medicines Quality Assurance Laboratory (NMQAL);

(iii) the Government Analyst or his nominee;

(*b*) nominated members-

(i) a Professor or a Senior Lecturer in Pharmacology of any University established under the Universities Act, No. 16 of 1978, nominated by the Deans of Medical Faculties;

(ii) a Professor or a Senior Lecturer in Pharmacy of any University in Sri Lanka established under the Universities Act, No.16 of 1978, nominated by the Deans of relevant Faculties of such Universities;

(iii) a Pharmacist of the Authority;

(iv) a Nutritionist from the Ministry of Health to be nominated by the Director General of Health Services;

(v) the Director of the Sri Lanka Standards Institute established under the Sri Lanka Standards Institute Act, No. 6 of 1984 or his nominee;

(vi) the Director of the Industrial Technology Institute or his nominee;

(vii) a representative from the Consumer Affairs Authority established under the Consumer Affairs Authority Act, No. 9 of 2003 nominated by the Chairman; and

(viii) a representative of Ayurveda Department nominated by the Commissioner of Ayurveda.

(2) The quorum for meetings shall be five members excluding the members of the Panel of Experts.

(3) The term of office of a nominated member shall be three years.

Panel of Experts.

91. (1) The Authority shall appoint a Panel of Experts, comprising of eminent professionals specialized in borderline products.

(2) The Authority may where necessary appoint additional members to the BPEC from the panel of experts, depending on the subject matter dealt with by the BPEC.

(3) The members appointed under subsection (2) shall be present at the meetings for which their presence is required and express their opinion but they shall have no voting rights at such meetings.

Declaration of secrecy.

92. Every member of the BPR division and the BPEC and all officers and employees of the BPR division and the BPEC shall, before entering upon duties, sign a declaration pledging to observe strict secrecy in respect of all matters connected with the affairs of the BPR division and the BPEC, which has come to his knowledge in the performance or exercise of his powers and functions under this Act and shall by such declaration pledge himself not to disclose any such matter, except—

(*a*) when required to do so by a court of law; or

(*b*) for the purpose of exercising or performing the powers and functions under this Act or any other written law.

Authority to give general guidelines for the evaluation.

93. (1) The Authority shall issue general guidelines to the BPEC for the evaluation of borderline products and other related items, submitted to the BPEC.

(2) (*a*) The general guidelines referred to in subsection (1), shall be based on the Good Manufacturing Practices (GMP) guidelines and other recommendations issued by the World Health Organization and other regulatory bodies recognized by the Authority.

(*b*) The Authority may revise the general guidelines from time to time in order to maintain parallels with internationally recognized standards and practices.

(3) The BPEC shall take into consideration the efficacy, safety, quality, need and cost of each borderline product, in the process of evaluation.

(4) The Minister may make regulations—

(*a*) setting out the procedures to be followed, including the specified time limits for the conduct of respective evaluations;

(*b*) to give effect to the Good Manufacturing Practices (GMP) guidelines and any other applicable guide lines as may be recommended by the Authority.

Application of certain provisions of this Act in relation to BPEC.

94. The provisions of sections 5, 6, 7, 8, 9, 10, 11, 12 and 13 of this Act shall *mutatis mutandis* apply to and in relation to the Chairman, members and the conducting of the affairs of the BPEC.

PART III

Offences Pertaining to Borderline Products

Prohibition of importation &c., of borderline products other than listed.

95. (1) The Authority shall list from time to time the borderline products registered under this Act.

(2) No person shall import, sell, transport, distribute or advertise any borderline product, other than a borderline product listed under subsection (1).

Regulation of manufacture, importation, sale and distribution of borderline products.

96. (1) No person shall import, distribute, re-pack or sell any borderline product which—

(*a*) is not manufactured, prepared, preserved, packaged or stored under good manufacturing practices and good storage practices;

(*b*) consists in whole or in part of any contaminant material, foreign body or decomposed substance or any foreign matter; or

(*c*) has in or upon it any substance that may cause injury to the health of the user when the borderline product is used—

(i) according to the directions on the label accompanying the borderline product; or

(ii) for such purposes and by such methods of use as are customary or usual in the use of that borderline product.

(2) No person shall label, package, treat, process, transport, distribute, sell, exhibit or advertise any borderline product in a manner that is false, misleading, deceptive or likely to create an erroneous impression regarding its efficacy, safety, quality or composition.

(3) No person shall manufacture any borderline product unless Good Manufacturing Practices (GMP) and Good Storage Practices (GSP) are complied with.

Where standard is prescribed for borderline products.

97. Where a standard is prescribed for borderline product, no person shall label, package, distribute or sell any such product which does not conform to that standard or in such a manner as is likely to be mistaken for the borderline product for which the standard has been prescribed.

Advertising, importation, sale and distribution of borderline products for prescribed diseases prohibited.

98. (1) No person shall advertise or promote or distribute any borderline product without prior written approval of the Authority.

(2) No person shall advertise or promote any borderline product to the public as a treatment, prevention or cure for any of the prescribed diseases, disorders or abnormal physical states.

(3) No person shall without prior written approval of the Authority import, sell or distribute any borderline product to the general public as a treatment, prevention or cure for any of the prescribed diseases, disorder or abnormal physical states.

Possession of prohibited borderline product.

99. No person other than the persons as may be prescribed by regulations shall obtain or have in his possession any prohibited borderline product which is not safe for general use.

Contravention of the provisions of this Part to be an offence.

100. Any person who contravenes any of the provisions specified in this Part of this Act commits an offence.

PART IV

Registration and Licensing of Borderline Products

Requirement to register &c., of borderline products.

101. (1) No person shall manufacture or import any borderline product without registering such borderline product with the Authority and obtaining a licence from the Authority therefor.

(2) No person shall store, assemble, re-pack, distribute, transport or sell any borderline product without obtaining a licence for that purpose from the Authority.

(3) Any person who contravenes any provision specified in subsection (1) or (2) of this section commits an offence.

Application for Registration of a borderline product.

102. (1) Any person who wishes to import, sell, manufacture, prepare or distribute any borderline product shall make an application for the registration of that borderline product in the prescribed form to the Authority.

(2) The application shall be accompanied by the prescribed particulars, the samples of the borderline products and the prescribed fee.

(3) (*a*) The Authority shall maintain a register in which every application received for the registration and licensing of a borderline product shall be recorded.

(*b*) The particulars to be entered in such register shall be as prescribed.

(4) The Authority shall upon receipt of an application submit the application together with the sample of the borderline products and all particulars, available -

(*a*) to the BPEC, for the evaluation of the application and the borderline products considering the need to ensure the availability of efficacious, safe and good quality borderline products relevant to the healthcare needs of the public at an affordable price; and

(*b*) to the NMQAL or where necessary any other laboratory for testing of the quality of the borderline product.

(5) The Authority shall inform the applicant in writing of the receipt of the application.

(6) The Minister may make regulations -

(*a*) setting out the procedures to be followed, by the BPEC and the NMQAL in their respective evaluation and testing processes;

(*b*) specifying –

(i) the time-limits in conducting such testing or evaluation;

(ii) the manner in which the BPEC to conduct its meetings and the procedure to be followed at such meetings; and

(iii) the matters which should be included in the reports to be submitted.

(7) (*a*) The Authority may require the BPEC and the NMQAL to finalize the testing or evaluation within a specified time period considering the urgency of the borderline product for the national health.

(*b*) The BPEC and the NMQAL shall within the time limits specified submit their reports to the Authority unless there are compelling reasons for any delay.

Registration of borderline products.

103. (1) (*a*) The Authority may where necessary, call for clarifications from the BPEC, NMQAL or any other expert, with regard to the reports submitted by the BPEC and the NMQAL.

(*b*) The Authority may upon taking into consideration the reports submitted by the BPEC, NMQAL and all other relevant factors register such borderline product or refuse the registration, within the stipulated time period.

(2) Where the Authority registers the borderline product, such registration shall be informed to the applicant in writing and may inform the public of such registration by Order published in the *Gazette*.

Refusal of Registration.

104. Where the Authority refuses the registration of the borderline product, such refusal shall be informed to the applicant with reasons therefor within the stipulated time period and shall inform the public of such refusal by Order published in the *Gazette*.

Application of the provisions of sections 62, 63, 64 and 65.

105. The provisions of sections 62, 63, 64 and 65 of this Act shall *mutatis mutandis* apply to and in relation to the —

(i) issuing of certificate of registration;

(ii) issuing of licence;

(iii) renewal of registration and licence; and

(iv) cancellation or suspension of registration or licence,

under this part of this Act.

CHAPTER VI

COLLECTIVE PROVISIONS PERTAINING TO MEDICINES, MEDICAL DEVICES AND BORDERLINE PRODUCTS

PART I

COMMON PROVISIONS

Prohibition of dishonest dealings.

106. (1) No person shall store, re-pack, assemble, transport, distribute or sell any illegal, counterfeit or smuggled, medicine, medical device or borderline product.

(2) (*a*) No person shall import, distribute, re-pack, display or sell any medicine, medical device or borderline product after the expiry date of such medicine, medical device or borderline product.

(*b*) No person shall store any medicine, medical device or borderline product after the expiry date of such medicine, medical device or borderline product except under conditions stipulated by the Authority.

(3) No person shall without lawful authority import, store, assemble, transport, distribute, re-pack, display or sell any medicine, medical device or borderline product containing the State logo or any other mark indicating that such products are a State property.

Authority to decide residual shelf-life of medicines &c.

107. (1) The Authority shall, decide the residual shelf-life of every medicine, medical device or borderline product imported into Sri Lanka at the port of entry.

(2) It shall be the responsibility of the importer to ensure quality, safety and efficacy of every medicine, medical device or borderline product imported by him.

Ban or withdrawal &c.,from, use of medicine &c.

108. (1) The Authority shall, where the Authority finds that any medicine, medical device or borderline product does not meet the required standard or that the medicine, medical device or the borderline product as manufactured would cause serious health problems to the person using, issue an order requiring the importer, manufacturer, trader or distributor of that medicine, medical device or borderline product to –

(*a*) cease the distribution immediately;

(*b*) withdraw from sale or use;

(*c*) notify immediately the health professionals and users to cease using of;

(*d*) dispose according to prescribed methods,

such medicine, medical device or borderline product.

(2) The Authority shall cause notice of the ban or withdrawal from use of medicine, medical device or borderline product in terms of this section, to be published in a daily newspaper in Sinhala, Tamil and English or website of the Ministry or broadcast over any electronic media.

(3) Any person who contravenes the provisions of subsection (1) commits an offence and shall on conviction by a Magistrate's Court after summary trial, be liable to a fine not exceeding one million rupees or to an imprisonment of either description for a period not exceeding three years or to both such fine and imprisonment.

Emergency and other special circumstances.

109. (1) The Authority may grant permission in special circumstances such as to save a life, to control an outbreak of an infection or an epidemic or any other national

emergency or for national security to import and supply a particular medicine, medical device or borderline product in specified quantities.

(2) Such permission may be granted:—

(*a*) on a request made by the Ministry of Health; or

(*b*) on a request made by an individual or an organization recommended by the Ministry of Health.

(3) The importer shall be responsible for the accountability and management of the medicine, medical device or borderline product imported under this section.

(4) The importer shall submit routine reports in the prescribed manner to the Authority, on the medicine, medical device or borderline product imported under this section.

Sale or distribution of samples of medicine &c., to be prohibited.

110. (1) (*a*) No person shall distribute any medicine, medical device or borderline product marked as Physician's sample to the general public.

(*b*) The provisions of paragraph (*a*) shall not apply to the distribution of any medicine, medical device or borderline product marked as physician, sample by a Medical Practitioner, Dentist or Veterinary Surgeon to a patient of such Medical Practitioner, Dentist or Veterinary Surgeon.

(2) (*a*) No person shall transport, exhibit or store any medicine, medical device or borderline product marked as a Physician's sample.

(*b*) The provisions of paragraph (*a*) shall not apply to any representative of a company duly authorized by the Authority.

(3) No person shall sell any medicine, medical device or borderline product marked as a physician's sample.

Permission to import and to accept as a donation of any medicine &c.

111. (1) Subject to the provisions of subsection (3) no person shall import or accept as a donation any medicine, medical device or borderline product for free distribution or to promote within Sri Lanka, without the approval of the authority.

(2) The provisions of subsection (1) shall apply to the importation or receiving of medicine, medical device or borderline product as a donation during an emergency or disaster situation.

(3) Minister may, prescribe the guidelines, for accepting donations of medicines, medical devices or borderline products at any disaster or emergency situation, taking into consideration the guidelines of the World Health Organization issued in relation to accepting or receiving medicines, medical devices or borderline products during similar situations.

Importation &c., of medicines &c., for personal use.

112. (1) The provisions of sections 58, 82 and 101 shall not apply to any patient who needs for his personal medication a medicine, medical device or borderline product which is not registered and licensed under this Act.

(2) Such person may import the required quantity of such medicine, medical device or borderline product on a prescription issued by the medical practitioner treating him, with the prior approval of the Authority.

(3) It shall be an offence to sell any medicine, medical device or borderline product manufactured or imported under this section.

Licensing of premises for manufacturing &c., of medicine &c.

113. (1) No person shall manufacture, prepare, store or sell any medicine, medical device or borderline product in any premises unless such premises has been licensed in that regard by the Authority.

(2) (*a*) No person shall store or sell any medicine, medical device or borderline product, in any premises unless such premises has been licensed by the Authority.

(*b*) The provisions of paragraph (*a*) shall not apply to—

(i) any patient who keeps any medicine, medical device or borderline product registered under this Act, for his personal use;

(ii) any medicine, medical device or borderline product prescribed by regulations as safe for general use.

(3) The Authority shall maintain a register of registered manufacturers and importers and the criteria for registering shall be as prescribed.

Conditions &c., pertaining to licence.

114. (1) Every licence granted under this Act shall—

(*a*) be in such form as may be prescribed;

(*b*) be subject to such conditions as may be prescribed;

(*c*) unless cancelled earlier, be in force for such period as may be specified in such licence.

(2) A licence granted under this Act may be suspended or revoked by the Authority in case of non-compliance with the prescribed conditions.

(3) An applicant may at any time withdraw an application for a licence by notifying the Authority in writing, without prejudice to his right to re-apply for a licence.

PART II

Regulation of Manufacturing of Medicines, Medical Devices and Borderline Products

Establishment of the Manufacturing Regulatory Division.

115. (1) The Authority shall establish for the purpose of this Act a Division to be known as Manufacturing Regulatory Division.

(2) The Authority shall appoint the head of that Division from among persons holding a recognized degree in Pharmacology, Pharmacy or any other related subject.

Functions of the Manufacturing Regulatory Division.

116. (1) The principal function of the Manufacturing Regulatory Division shall be the regulation of manufacturing of medicines, medical devices and borderline products in Sri Lanka.

(2) The other functions of the Manufacturing Regulatory Division shall be to—

(*a*) formulate schemes to provide all necessary assistance including technical knowhow to the prospective manufacturers;

(*b*) provide necessary assistance to the manufacturers to market their products locally;

(*c*) provide necessary assistance to manufacturers to export their products;

(*d*) advise the Authority to restrict the importation of certain products where locally manufactured products are sufficiently available in Sri Lanka.

(3) For the purpose of this section "product" means a medicine, medical device or borderline product.

Regulations.

117. Minister may make regulations to give effect to all or any of the provisions of this Part of this Act.

PART III

PRICING OF MEDICINES, MEDICAL DEVICES AND BORDERLINE PRODUCTS

Pricing of medicines &c.

118. (1) (*a*) The Authority shall appoint a Committee to be known as the Pricing Committee.

(*b*) The composition, powers and functions of the Pricing Committee shall be as prescribed.

(2) (*a*) The Authority shall in consultation with the Pricing Committee, determine the introductory price of medicines, medical devices and borderline products at the time of registration, based on the criteria as may be prescribed.

(*b*) For the purpose of paragraph (*a*), the Authority shall consider the prevailing market prices of similar products within the same therapeutic class, International Reference Prices and other factors as may be prescribed.

(3) For the purpose of determining the prices of New Chemical Entities, the Authority shall consider the prices in the region, the benefit of the new product and the cost effectiveness.

(4) The Minister shall in consultation with the Pricing Committee, the Consumer Affairs Authority and all stakeholders and taking into consideration all other relevant factors including the provisions of the Consumer Affairs Authority Act, No. 9 of 2003, prescribe a pricing mechanism for medicines, medical devices and borderline products.

CHAPTER VII

MISCELLANEOUS

PART I

REGULATION OF PHARMACIES

Every person to carry on a Pharmacy to obtain a licence.

119. (1) No person shall carry on a Pharmacy without obtaining a licence from the Authority.

(2) Any person who intends to carry on a Pharmacy shall make an application for that purpose in the prescribed form to the Authority.

(3) The application shall contain all such information and be forwarded with all such documents as may be set out in such form and be accompanied by the prescribed fee.

(4) The Authority may on receipt of an application refer the application to the Pharmacies Regulatory Division for their observations which shall be submitted within a specified time period.

(5) The Authority may upon consideration of all records and information pertaining to the application,

(*a*) grant the applicant the licence; or

(*b*) refuse the application and inform the reason for such refusal to the applicant in writing forthwith.

(6) The holder of a licence shall before the commencement of the business of a Pharmacy shall register the premises where the Pharmacy is to be carried on.

(7) The Minister shall by regulations prescribe the terms and conditions of a licence and the conditions to be satisfied to register a Pharmacy.

(8) For the purpose of this part of this Act, "holder of licence" means the person granted a licence to carry on a Pharmacy under this section.

Requirement to comply with Good Pharmacy Practices.

120. (1) Every person who carries on a Pharmacy shall comply with Good Pharmacy Practices and other guidelines and conditions prescribed by the Authority.

(2) The holder of licence shall employ at least one Pharmacist in the pharmacy to be responsible for all operations of the Pharmacy relating to medicines, medical devices or borderline products.

(3) The dispensing of medicines, medical devices or borderline products shall be carried out by the Pharmacist or a registered apprentice Pharmacist under the direct supervision of the Pharmacist.

(4) The Pharmacist shall before the sale of every medicine, medical device or borderline product, inform the buyer the cost of such medicines, medical device or borderline products.

(5) The Pharmacist shall when dispensing the medicine, medical device or borderline product provide the customer with a description of such medicine, medical device or borderline product, in the language requested for by such customer.

Regulations.

121. Minister may make regulations to give effect to all or any of the provisions of this Part of this Act.

PART II

APPEALS

Appeals.

122. (1) (*a*) Any person aggrieved by any decision of the Authority made under this Act may appeal in writing to the Authority to reconsider such decision within one month of the receipt of such decision.

(*b*) The Authority shall as soon as practicable inform its decision on such appeal to the appellant.

(2) Where the appellant is dissatisfied with the decision of the Authority, the appellant may appeal against such decision to the Appeals Committee appointed under section 123.

The Appeals Committee.

123. (1) The Minister shall appoint an Appeals Committee to hear and determine appeals made in terms of this Act.

(2) The Appeals Committee shall consist of the following–

(*a*) a member appointed from among retired judges of the Supreme Court or the Court of Appeal of Sri Lanka who shall be the Chairman of the Appeals Committee;

(*b*) the Secretary of Health; and

(*c*) a member appointed from among retired Medical Consultants who has distinguished himself in the field of medicine.

(3) The members of the Appeals Committee shall hold office for a term of three years from the date of appointment, and shall be eligible for reappointment.

(4) The Minister may make regulations specifying the manner in which the meetings and business of the Appeals Committee shall be carried out.

(5) The Appeals Committee may, after studying the appeal, call for further information regarding the medicine, medical device or borderline product in question from the appellant and respective Divisions established under this Act and may call for expert opinion on such medicine, medical device or borderline product.

(6) The Appeals Committee shall on consideration of all relevant factors inform its decision to the Authority.

(7) Upon receiving the decision of the Appeals Committee, the Authority shall inform the appellant the decision of the Appeals Committee forthwith and act in accordance with the decision of the Appeals Committee.

(8) The members of the Appeal Committee may be paid such remuneration out of the Fund of the Authority with the concurrence of the Minister assigned of the subject of Finance.

PART III

POWERS AND FUNCTIONS OF THE AUTHORIZED OFFICERS

Authorized Officers.

124. (1) The Minister may appoint any Provincial Director of Health Services, any Regional Director of Health Services, any Medical Officer of Health, any Divisional Pharmacist, any Food and Drugs Inspector, Drugs Inspector or any Pharmacist attached to the Authority to be an "Authorized Officer" for the purposes of this Act.

(2) Every Authorized Officer shall exercise the powers of a peace officer in terms of the Code of Criminal Procedure Act, No. 15 of 1979, for the purpose of discharging his functions under this Act.

(3) Any Authorized officer who-

(*a*) acts in contravention of the provisions of this Act or any regulation or rule made thereunder or the provisions of any other written law; or

(*b*) exercises the powers assigned to him under this Act in a manner or for an intention contrary to the objects of this Act, shall after a due inquiry held by a disciplinary committee appointed by the Minister, be removed from such office.

(4) The Minister shall by regulations, prescribe the constitution of the disciplinary committee and manner of conducting an inquiry.

Powers of Authorized Officers.

125. (1) An Authorized Officer, for the performance of his duties and the exercise of his powers under the Act may-

(*a*) enter at any reasonable hour to any place where he believes any article is manufactured, prepared, packaged, re-packed, preserved, sold or stored and examine any such article and take samples thereof, and examine anything that he believes is used for the manufacture, preparation, packaging, preservation or storing of such article;

(*b*) open and examine any receptacle or package that he believes to contain any article;

(*c*) for the purposes of examining or search, stop or detain any vehicle in which he believes that any article is being conveyed, search that vehicle and examine such article and take samples of the said article;

(*d*) examine any book, document or other records including electronic data found in any place referred to in paragraph (*a*) and make copies thereof or take extracts therefrom; and

(*e*) seize and detain for such time as may be necessary, any article or vehicle by means of or in relation to which he believes any provisions of this Act or regulations made thereunder have been contravened.

(2) An Authorized Officer acting under this section shall if so required, produce his authority.

(3) The owner or person in charge of a place entered by an Authorized Officer in pursuance of subsection (1) and every person found therein shall give the Authorized Officer all reasonable assistance in his power and furnish him with such information and such samples as he may require.

(4) No person shall obstruct any Authorized Officer acting in the exercise of his powers under this Act or any regulation made thereunder.

(5) Where any Authorized Officer applies to obtain samples of any article exposed for sale, and the person exposing the article refuses to sell to the Authorized Officer such quantity thereof as he may require or refuses to allow that officer to take the quantity which he is empowered to take as samples, the person so refusing shall be deemed for the purposes of subsection (4) to have obstructed an Authorized Officer.

(6) No person shall knowingly make a false or misleading statement either orally or in writing to any Authorized Officer engaged in the exercise of his powers under this Act or any regulation made thereunder.

(7) No person shall remove or alter, tamper or otherwise interfere in any manner with any article seized under this Act by an Authorized Officer, without the authority of the Authorized Officer.

(8) Any article seized under this Act may, at the option of the Authorized Officer, be kept or stored in the building or place where it was seized or may at his discretion be removed to any Government Institution functioning under the Ministry of Health or the Provincial Health Services.

(9) An Authorized Officer shall inform the Authority of any seizure made under this Act as soon as practicable.

Procedure in respect of articles and vehicles seized.

126. (1) Upon the receipt of any information under section 125 (9) where the Authority is satisfied that there has not been a contravention of any of the provisions of this Act or any of the regulations made thereunder-

(*a*) the Authority shall direct the Authorized Officer to release such article and vehicle;

(*b*) where the owner of such article or the person in possession of such article at the time of seizure-

(i) consents in writing for the destruction of such article, the Authority shall direct destruction or disposal of such article and release of the vehicle;

(ii) does not consent in writing to the destruction of such article, the Authority shall direct the Authorized Officer, with notice to such person in possession of the article and the owner of such vehicle, to make a complaint to the Magistrate's court having jurisdiction over the area in which the offence was committed of the seizures of the article or the vehicle in respect of which the offence was committed.

(2) On complaint being made to the court under subsection (1) (*b*), such court shall, after trial, if found the owner or person in possession of the article-

(*a*) guilty of contravening any of the provisions of this Act or regulations made thereunder, order that such

article be forfeited to the Authority to be disposed of, as the court may direct:

Provided however, that where the offender is not known or cannot be found, such article shall be forfeited to the Authority without the institution of proceedings in respect of such contravention; or

(*b*) not guilty of contravening any of the provisions of this Act or regulations made thereunder, order that such article be released to such owner or person in possession thereof.

Authorized Officer to produce before court the part of the sample retained by him.

127. (1) Where a sample obtained by an Authorized Officer is required to be divided by him into parts, one of which shall be retained by him and the part retained by him shall be produced in court at the commencement of the trial of the prosecution in relation to such sample.

(2) The Magistrate may on his own motion and shall, at the request of any party to the prosecution, forward for analysis or examination such part of the sample produced in court under subsection (1), to the Approved Analyst.

(3) The Approved Analyst to whom such part of the sample is forwarded under subsection (2) shall send his report or certificate to the court within twenty eight days of the receipt by him of such part of the sample.

(4) The expenses of the analysis or examination shall be paid by such party as the court may direct.

Copy or extract of document taken by an Authorized Officer.

128. A copy made or extract taken from any book, document or record by an Authorized Officer under section 125(1) (d) shall, if certified to be a true copy or extract by the Authorized Officer, be admissible in evidence against the person keeping or maintaining that book, document or record or causing that book, document or record to be kept or maintained and shall be prima facie evidence of the contents of that book, document or record.

Analysis.

129. (1) An Authorized Officer shall submit any article seized by him or any portion thereof or any sample taken by him to the Authority and, unless destroyed under section 126 (1), to the Approved Analyst for analysis or examination, as decided by the Authority.

(2) Where the Approved Analyst has made an analysis or examination of the article submitted to him under subsection (1), he shall issue a certificate or report to the Authority and to the relevant authorized officer setting out in that certificate or report the results of his analysis or examination.

(3) For the purposes of this part of this Act-

"Approved Analyst" includes an Additional Approved Analyst; and

"article" means medicine, medical device or borderline product.

PART IV

General Offences

General offences.

130. Every person who—

(*a*) being a person acting under the authority of this Act, discloses any information obtained by him in or in connection with the exercise of his powers or the discharging of his functions under this Act, to any person for any purpose other than a purpose for which he is authorized to disclose such information;

(*b*) obstructs, without any justifiable or lawful basis, any person acting in the exercise of his powers under this Act or any regulation made thereunder;

(*c*) being a person acting under the authority of this Act, behaves or conducts himself in a vexatious or

provocative manner, while exercising or discharging any power or function under this Act; or

(*d*) fails to furnish any return or information in compliance with any requirement imposed on him under this Act or knowingly makes any false statement in any return or information furnished by him,

shall be guilty of an offence under this Act.

Punishment for the contravention of the provisions of this Act.

131. (1) Every person who contravenes any of the provisions of this Act or any regulation made thereunder shall be guilty of an offence and shall on conviction be liable—

(*a*) where the nature of the offence involves injury to the health of the public, to a fine not exceeding two hundred thousand rupees or to imprisonment for a term not exceeding three years or to both such fine and imprisonment;

(*b*) for unauthorized use of State logo or any other mark which indicates that a medicine, medical device or borderline product to be state property, to a fine not exceeding one hundred thousand rupees or to imprisonment for a term not exceeding three years or to both such fine and imprisonment;

(*c*) for carrying on a Pharmacy without obtaining a licence from the Authority, to a fine not exceeding one hundred thousand rupees or to imprisonment for a term not exceeding three years or to both such fine and imprisonment;

(*d*) for any other offence –

(i) for the first offence, to a fine not exceeding one hundred thousand rupees or to

imprisonment for a term not exceeding three months or to both such fine and imprisonment;

(ii) for a second or subsequent offence, to a fine not exceeding two hundred thousand rupees or to imprisonment for a term not exceeding six months or to both such fine and imprisonment;

(*e*) to publish an apology in addition to the punishment mentioned in paragraphs (*a*), (*b*), (*c*) and (*d*) to the general public in one Sinhala, Tamil and English newspaper each, circulating in Sri Lanka substantially in the size of 10"x 10" in front page to the effect that he shall not repeat the offence.

(2) Where a person convicted of an offence under this Act or any regulation made thereunder is convicted of a second or subsequent, offence of a like or similar nature under this Act or regulations made thereunder, the court convicting him for the second or subsequent offence may -

(*a*) cause the name and address of the person convicted and the offence and the punishment imposed for such offence to be published in such newspaper or in such other manner as the court may direct and recover the cost of publication from the person convicted as if it were a fine imposed on him;

(*b*) cancel any licence or registration issued to the person convicted for the manufacture, importation, sale and distribution of any medicine, medical device or borderline product under this Act or any other law and inform the relevant licensing Authority accordingly.

(3) Where a person is convicted of an offence under this Act or the regulations made thereunder relating to the storage, sale, distribution and transportation of any illegal,

unregistered, counterfeit and smuggled medicine, medical device or borderline product which is marked state logo or any other marking indicating that such medicine, medical device or borderline product is state property, the Magistrate may, in addition to the punishment provided under this Act, upon application made by an Authorized Officer for closure of such premises, order the closure of such premises or discontinuance of trade or business carried on therein.

(4) Where such person fails to comply with the order issued under this section, the Magistrate shall forthwith issue an order to the Fiscal of such Court requiring and authorizing such Fiscal to close such premises and discontinue the trade or business carried on therein before a date specified in the order, not being a date earlier than three days and not later than seven days from the date of issue of such order.

Person committing offence to be arrested without a warrant and to be tried by a Magistrate's Court.

132. Every person who commits an offence under this Act or any regulation made thereunder may be arrested without a warrant and every offence under this Act or regulations made thereunder shall be triable by a magistrate Court.

Where the accused proves that some other person is guilty of the offence.

133. (1) Where a person (hereinafter referred to as "the accused") is charged with an offence under this Act, he shall, upon complaint duly made by him in accordance with the provisions of section 136 of the Code of Criminal Procedure Act, No. 15 of 1979, and on giving to the prosecution not less than three days' notice of his intention, be entitled to have any other person whom he charges as the actual offender brought before the court, and if, after the commission of the offence has been proved, the accused proves to the satisfaction of the court that the commission of the offence was due to the act or default of such other person, such other person may be convicted of the offence, and, if the accused further proves that he has used all due diligence to enforce the provisions of this Act, he shall be acquitted of the offence.

(2) Where an accused seeks to avail himself of the provisions of subsection (1)—

(*a*) the prosecution, as well as the person whom the accused charges with being the actual offender, shall have the right to cross-examine him, if he gives evidence and any witness called by him in support of his pleas, and to call evidence in rebuttal; and

(*b*) the court may make such order as it thinks fit for the payment of costs by any party to the proceedings to any other party thereto.

Defence.

134. (1) In a prosecution for the offence of sale of any medicine, medical device or borderline product contrary to the provisions of this Act or any regulation made thereunder, subject to subsection (2) it shall be a defence for the accused—

(*a*) that he purchased the medicine, medical device or borderline product in a package and sold it in the same package and in the same condition that it was at the time he purchased it; and

(*b*) that he could not have with reasonable diligence, ascertained that the sale of the medicine, medical device or borderline product would be in contravention of the Act or any regulation made thereunder.

(2) The defence specified in subsection (1) shall not be available to an accused unless he has within thirty days of the detection of the offence informed in writing to the Authorized Officer detecting the offence—

(*a*) of his intention to avail himself of such defence; and

(*b*) the name and address of the person from whom he purchased the medicine, medical device or borderline product and the date of purchase.

Presumptions.

135. (1) For the purposes of this Act and of any regulations made thereunder—

(*a*) any medicine, medical device or borderline product found, kept or exhibited in any shop or other place commonly used for the sale of articles shall be presumed until the contrary is proved to be intended for sale; and

(*b*) any substance capable of being used in the composition or preparation of any medicine, medical device or borderline product which is found in the premises and used in a preparation shall be presumed until the contrary is proved, to be intended for use in the composition or preparation of that medicine, medical device or borderline product.

(2) Where in a prosecution for the offence of manufacturing a medicine which is adulterated, it is established –

(*a*) that such medicine was adulterated with the addition of any other substance; and

(*b*) that the accused had in his possession or premises such other substance,

it shall be presumed until the contrary is proved that such medicine was adulterated by the addition of that other substance.

(3) Where a package containing any medicine, medical device or borderline product has on or upon it the name and address purporting to be the name or address of the person who manufactured or packaged it, it shall be presumed until the contrary is proved that the medicine, medical device or borderline product was manufactured or packaged, as the case may be, by the person whose name or address appears on the package.

Offence committed by body of persons.

136. Where an offence under this Act or any regulation made thereunder is committed by a body of persons and-

(*a*) if that body of persons is a body corporate, every person who at the time of commission of the offence was a Director, General Manager, Secretary or other similar officer of that body; or

(*b*) if that body is not a body corporate, every person who at the time of commission of the offence was a member of that body,

shall be deemed to be guilty of that offence, unless he proves that such offence was committed without his consent or concurrence and that he exercised all due diligence to prevent the commission of such offence as he ought to have exercised in the circumstances having regard to the nature of his functions.

PART V

GENERAL

Approved Analyst.

137. (1) For the purposes of this Act and the regulations made thereunder the Government Analyst shall be the Approved Analyst.

(2) The NMQAL and the Medical Research Institute shall be the Additional Approved Analysts.

(3) Notwithstanding the provisions of subsections (1) and (2), the Minister may approve any other laboratory or institution recommended by the Authority to be an Additional Approved Analyst and notification of the approval shall be published in the *Gazette*.

(4) No person, laboratory or institution shall be approved as an Additional Approved Analyst-

(*a*) if that person, the laboratory or institution does not possess the prescribed qualifications or facilities as the case may be; or

(*b*) if that person is engaged directly or indirectly in any trade or business connected with the manufacture, importation, sale or distribution of medicine, medical device or borderline product.

Report or certificate of the Approved Analyst or an Additional Approved Analyst.

138. (1) In the absence of evidence to the contrary, a document purporting to be a report or a certificate signed by the Approved Analyst or an Additional Approved Analyst upon any matter submitted to him for analysis or examination shall be sufficient evidence of the facts stated therein.

(2) When a party against whom a report or a certificate referred to in subsection (1) is produced, requests the Approved Analyst or an Additional Approved Analyst, to be summoned as a witness, the court shall summon him, upon that party depositing in court the expenses of summoning him including such fees as may be prescribed, payable to him and shall examine him as witness.

(3) The report or the certificate referred to in subsection (1) shall not be received in evidence unless the party intending to produce it has given the party against whom it was intended to be produced a copy of the report or the certificate and reasonable notice of his intention to produce it.

Priority for trial and appeal under this Act.

139. Every Court shall give priority to the trial of any person charged with, or indicted for, any offence under this Act and to the hearing of any appeal from the conviction of any such offence and sentence imposed on such conviction.

Application of other written laws.

140. (1) The provisions of this Act and any regulation made thereunder relating to medicine which are excisable articles within the meaning of the Excise Ordinance (Chapter 52) shall be in addition to and not in substitution for the provisions of that Ordinance.

(2) The provisions of the Customs Ordinance (Chapter 235) shall apply for the purpose of the enforcement, and the prevention and punishment of contraventions or attempted

contraventions of the provisions of this Act and any regulation made thereunder relating to the importation of any medicine, medical device or borderline product.

(3) For the purposes of the application of the Customs Ordinance to any medicine, medical device or borderline product the importation of which is prohibited under this Act, medicine, medical device or borderline product shall be deemed to be goods the importation of which is prohibited under that Ordinance.

PART VI

RULES AND REGULATIONS

Rules.

141. (1) Subject to the provisions of this Act the Authority may make rules in respect of all matters for which rules are authorized or required to be made under this Act.

(2) Every rule made by the Authority shall be approved by the Minister and be published in the *Gazette* and shall come into operation on the date of its publication or on such later date as may be specified therein.

Regulations.

142. (1) The Minister may make regulations in respect of any matter required by this Act to be prescribed or in respect of which regulations are authorized by this Act to be made.

(2) In particular and without prejudice to the generality of the powers conferred by subsection (1), the Minister may make regulations in respect of all or any of the following matters:-

(*a*) declaring that any medicine, medical device or borderline product or class of medicine, medical device or borderline product is adulterated if any prescribed substance or class of substance is present or has been added to or extracted from or omitted in, that medicine, medical device or borderline product;

(*b*) declaring that any medicine, medical device or borderline product is safe for general use or not safe for general use;

(*c*) pricing of medicines, medical devices and borderline products;

(*d*) the labeling and packaging and the offering, exposing and advertising for sale of medicine, medical device or borderline product;

(*e*) prescribing the size, dimensions, fill and other specifications of packages of, medicine, medical device or borderline product;

(*f*) the use of any substance as an ingredient in medicine, medical device or borderline product to prevent the user or purchaser from being deceived or misled as to its quality, character, value, composition or to prevent injury to the health of the user or purchaser;

(*g*) the standards of composition, strength, potency, purity, quality or other property of medicine, medical device or borderline product;

(*h*) the method of preparation, the manufacture, preservation, packaging, storing and testing of any medicine in the interest of, or for the prevention of injury to, the health of the user or purchaser;

(*i*) (i) the persons to whom, the circumstances in which, and the terms and conditions subject to which, licences and registrations under this Act may be granted or refused; and

(ii) the manner and mode in which applications for licences and registrations under this Act may be made and dealt with;

(*j*) requiring persons who manufacture or sell any medicine, medical device or borderline product to furnish information and maintain books and records;

(*k*) the registration and regulation of Pharmacies and drug stores;

(*l*) the terms and conditions for storage and transport of medicine, medical device, borderline product or investigational medicinal product;

(*m*) the disposal of medicine, medical device, borderline product or investigational medicinal product;

(*n*) the specification of recalling procedure of medicines, medical devices and borderline products and composition of committees;

(*o*) the conditions relating to importers and market authorization holders;

(*p*) the procedure for parallel imports and licensing for non-commercial use by the Government;

(*q*) Forms to be used for the registration, renewal and licensing under this Act and the regulations made thereunder;

(*r*) prohibition and restrictions relating to the sale and transport for sale of any adulterated medicine or borderline product;

(*s*) prescribing the medicines, medical devices or borderline products prohibited under the Act;

(*t*) the distribution and the conditions of distribution of sample of any medicine, medical device, borderline product or investigational medicinal product;

(*u*) the mode and manner in which any medicine, medical device or borderline product shall be registered, the terms and conditions applicable to such registration and licensing, the fees to be levied for such registration or licensing;

(*v*) the manner in which the Appeal Committee shall function and procedure of hearing Appeals;

(*w*) the standards of shelf-life for manufacture of medicines, medical devices or borderline products;

(*x*) procedure to be followed by the MEC, MDEC and BPEC in the conduct of its functions and the transaction of its business;

(*y*) the procedure of inquiries;

(*z*) the procedure to be followed by MEC, MDEC and BPEC for the respective evaluations and matters which should be included in reports;

(*aa*) the review and revision of all guidelines formulated under this Act;

(*bb*) the procedure for issuing of lot release certificate by Medical Research Institute in relation to vaccines and sera;

(*cc*) evaluation of advertisements and other promotional material of manufacturers, importers, distributors and retailers of medicines, medical devices and borderline products;

(*dd*) regulation of promotional activities pertaining to medicines, medical devices, borderline products and investigational medicinal products;

(*ee*) any other matters as may be necessary for the purposes of achieving the objects and discharging the functions of the Authority.

(3) Every regulation made by the Minister shall be published in the *Gazette* and shall come into operation on the date of such publication or on such later date as may be specified in such regulation.

(4) Every regulation made by the Minster, shall not later than three months after its publication in the *Gazette,* be brought before Parliament for approval. Any regulation which is not so approved shall be deemed to be rescinded as from the date of such disapproval, but without prejudice to anything previously done thereunder.

(5) A notification of the date of such disapproval shall be published in the *Gazette.*

Institution of proceedings.

143. (1) A prosecution for an offence under this Act or any regulation made thereunder shall not be instituted-

(*a*) except by an Authorized Officer; and

(*b*) after the expiration of a period of three months from the date of detection of that offence or where sample is analysed, after the expiration of a period of one month from the date of the receipt of Analyst's report on such sample.

(2) No civil or criminal proceedings shall be instituted against person for any act which in good faith is done or purported to be done by him under this Act or any regulation make thereunder.

PART VII

Repeals and Transitional Provisions

Repeal of Act, No. 27 of 1980.

144. Cosmetics, Devices and Drugs Act, No. 27 of 1980 is hereby repealed.

Transitional provisions.

145. Notwithstanding the repeal of Cosmetics, Devices and Drugs Act, No. 27 of 1980 (hereinafter referred to as "the repealed Act"), -

(*a*) all contracts and agreements entered into under the repealed Act and subsisting on the day immediately preceding the appointed date shall, with effect from the appointed date, be contracts and agreements entered into under this Act with or on behalf of the Authority and may be enforced accordingly;

(*b*) all suits, prosecutions, appeals or other legal proceedings which have been instituted in any court or tribunal by or against the Cosmetics, Devices and Drugs Authority and pending before such court or tribunal on the day immediately preceding the appointed date shall with effect from the appointed date be deemed to have been instituted by or against the Authority and may be continued accordingly;

(*c*) all decrees, orders and judgments entered or made by a competent court or tribunal in favor of or against the Cosmetics, Devices and Drugs Authority and remaining unsatisfied on the day preceding the appointed date shall with effect from the appointed date be deemed to have been made in favor of or against the Authority, and may be enforced accordingly;

(*d*) every regulation or rule made under the repealed Act , and in force on the day immediately preceding the appointed date and not inconsistent with the provisions of this Act, shall with effect from the appointed date be deemed to have been made under this Act and may accordingly be amended or rescinded by regulations or rules made under this Act;

(*e*) every licence or registration issued by the Cosmetics, Devices and Drugs Authority and in force immediately prior to the date of operation of

this Act shall with effect from the appointed date be deemed to be a licence or registration granted by the Authority under the provisions of this Act;

(*f*) every application for a licence or registration of a medicine, medical device or borderline product made to the Cosmetics, Devices and Drugs Authority under the provisions of the repealed Act shall with effect from the appointed date be deemed to be an application made to the Authority established under this Act and shall be dealt with accordingly;

(*g*) all movable and immovable property vested in the Cosmetics, Devices and Drugs Authority on the day immediately preceding the appointed date, shall, with effect from the appointed date, be vested with the Authority;

(*h*) all sums of money lying to the credit of the fund of the Cosmetics, Devices and Drugs Authority on the day immediately preceding the appointed date, shall stand transferred, with effect from the appointed date, to the Fund established under section 18 of this Act;

(*i*) all declarations, notifications, licences and orders made or issued under the repealed Act and subsisting on the day immediately preceding the appointed date, shall in so far as they are not inconsistent with the provisions of this Act, be deemed with effect from the appointed date, to be declarations, notifications, licences and orders made or issued under the provisions of this Act and shall be construed accordingly;

(*j*) every reference to the Cosmetics, Devices and Drugs Authority in any written law, notice, notification, instrument, contract, communication or other

document shall with effect from the appointed date be read and construed as a reference to the Authority established under this Act; and

(*k*) every reference to the National Druge Quality Assurance Laboratory of the Cosmetics, Devices Drugs Authority in any written law, notice, notification, contract, communication or other document shall with effect from the appointed date be read and construed as a reference to the NMQAL of the Authority established under this Act.

PART VIII

INTERPRETATION

146. In this Act, unless the context otherwise requires:— Interpretation.

"adulterated" means the addition of any substance to or subtraction of any constituent from a medicine, medical device or borderline product so as to affect its quality, composition or potency;

"advertisement" includes any representation by any means whatsoever, for the purpose of promoting directly or indirectly the manufacture, sale or disposal of any medicine medical device or borderline product;

"article" means —

(*a*) any medicine, medical device or borderline product;

(*b*) anything used or capable of being used for the manufacture, preparation, preservation, packaging or storing of any medicine, medical device or borderline product ; and

(*c*) any labeling or advertising material;

"bioequivalence" means two pharmaceutically equivalent or pharmaceutical alternative products having their bio availabilities after administration in the same molar dose are similar to such a degree that their effects, with respect to both efficacy and safety, will be essentially the same. This is considered demonstrated if the 90% confidence intervals (90% CI) of the ratios for AUC_{0-t} and C_{max} between the two preparations lie in the range 80.00 – 125.00%;

"biowaiver" means a regulatory approval process when the application (dossier) is approved on the basis of evidence of equivalence other than an in vivo bioequivalence test. For solid oral dosage forms, the evidence of equivalence is determined on the basis of an in vitro dissolution profile comparison between the multisource and the comparator product;

"borderline products" means the products having combined characteristics of medicines and foods, medicines and medical devices or medicines and cosmetics and in deciding whether a product is a borderline product the following shall be taken into consideration:-

(*a*) the intended use of the product (or its primary function) and its mode of action;

(*b*) the therapeutic claims that the manufacturer makes about the product (claims to treat or prevent disease or to interfere with the normal operation of a physiological function of the human body);

(*c*) the pharmacological active substance(*s*), if any, used in the product;

(*d*) the concentration of the active substances;

(*e*) the level of efficacy of the active substance of the product; and

(*f*) the ingredients used and the concentrations at which they are used;

"Cosmetics" means any substance or mixture of substances manufactured, sold or represented for use in cleaning, improving or altering the complexion, skin, hair or teeth and includes deodorants, perfumes and cosmeceuticals;

"Cosmetics, Devices and Drugs Authority" means Cosmetics, Devices and Drugs Authority established under the Cosmetics, Devices and Drugs Act, No. 27 of 1980;

"counterfeit medical device" means a device which is labeled or packaged fraudulently with regard to identification;

"counterfeit medicine" means a medicine which is labeled or packaged fraudulently with regard to identification and includes any product with proper ingredients with inferior quality or containing different or inactive ingredients;

"dentist" means a person for the time being registered as a dentist under the Medical Ordinance (Chapter 105);

"Drug Inspector" mean any person with prescribed qualifications appointed as a drug inspector by the Authority;

"exhibit" refers to a public display of medicines, medical devices or borderline products at a conference, exhibition or trade fair;

"Generic medicine" means a medicine that-

(*a*) has the same quantitative composition of therapeutically active substances, being substances of similar quality to those used in the registered medicine;

(*b*) has the same pharmaceutical form;

(*c*) is bioequivalent; and

(*d*) has the same safety and efficacy properties;

"Good Distribution Practice" means good distribution practice guidelines issued by the Authority;

"Good Manufacturing Practice Guidelines" means good manufacturing guidelines issued by World Health Organization;

"Good Pharmacy Practice" means good Pharmacy practice guidelines issued by the Authority;

"Good Storage Practice" means good storage practice guidelines issued by the Authority;

"Government Analyst" means the person for the time being holding the office of the Government Analyst, any Additional Government Analyst, Deputy Government Analyst, Senior Assistant Government Analyst or Assistant Government Analyst;

"insanitary conditions" means such conditions or circumstances as are likely to contaminate medicine, medical device or borderline product with dirt or filth or render same injurious to health;

"investigational medicinal product" means a product which is under investigation by a clinical trial or equivalent studies which may include a medicine, medical device or a borderline product;

"label" includes any tag, brand, mark, pictorial or other descriptive matter, written, printed, stenciled marked, embossed or impressed on, or attached to a container of medicine, medical device or borderline product;

"labeling" includes the label and any written printed or graphic matter relating to and accompanying the medicine, medical device or borderline product;

"licence" means a licence issued under this Act;

"Medical Council" means the Medical Council established under the section 12 of the Medical Ordinance (Chapter 105);

"medical device" means any instrument, apparatus, appliance, software, material or any other article, whether used single or in combination, including the software necessary for its proper application intended by the manufacturer used in or on human beings for the purpose of:-

(*a*) diagnosis, prevention, monitoring, treatment or alleviation of disease;

(*b*) diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap;

(*c*) investigation, replacement or modification of the anatomy or of a physiological process;

(*d*) control of conception,

and which does not achieve its intended action in or on the human body by pharmacological, immunological or metabolic means but which may be assisted in its function by such means;

a medical device does not include an Ayurveda device or a Homeopathy device;

"medical practitioner" means a person registered as a medical practitioner under section 29 or section 41 of the Medical Ordinance (Chapter 105);

"medicine" means—

(*a*) any substance or mixture of substances manufactured, sold, offered for sale or represented for use in—

(i) the diagnosis, treatment, mitigation or prevention of disease, abnormal physical states or the symptoms thereof in man or animal; and

(ii) restoring, correcting or modifying functions of organs in man or animal;

(*b*) a medicine or combination of medicine ready for use and placed on the market under a special name or in a characteristic form, both patent and non-proprietary preparations;

(*c*) a product made out of medicinal herbal extract;

(*d*) nutraceutical with therapeutic claims; and

(*e*) vaccines and sera,

but does not include an Ayurvedic medicine or Homoeopathic medicine;

"Minister" means the Minister to whom the subject of Health is assigned and the term Ministry shall be construed accordingly;

"need" refers to circumstances in which a product is necessary because it is essential or very important rather than just desirable;

"nutraceutical" means a product isolated or purified from food which is generally sold in medicinal form not usually associated with food and provide physiological benefit or protection against chronic disease;

"package" includes anything in which any medicine, medical device or borderline product is wholly or partly contained, placed or packed;

"person" includes a company;

"Pharmacist" means a Pharmacist registered under the Medical Ordinance (Chapter105);

"prescribed" means prescribed by rules or regulations made under this Act;

"prescription" means an authorization in writing to a Pharmacist from a person authorized by law to prescribe medicines or medical devices to dispense a specified medicine or medical device for use by a designated individual or for animal use;

"prohibited medicine, medical device or borderline product" means which are prohibited by regulations made under the Act;

"secretary" means the Secretary to the Minister to whom the subject of Health is assigned;

"sell" means offer, keep or expose for sale, transmit, convey or deliver for sale, for cash or credit or by way of exchange and whether by wholesale or retail and the term "sale" shall be construed accordingly;

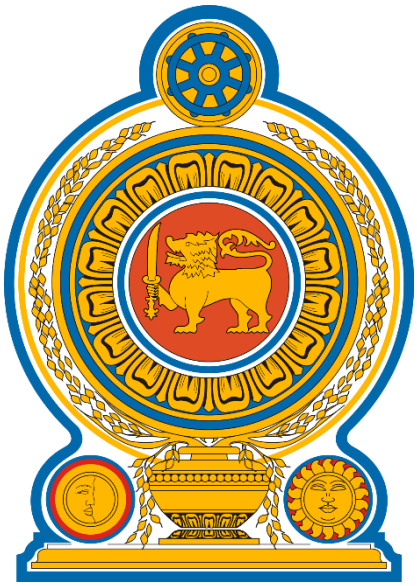
"smuggled medicine, medical device or borderline product" means a medicine, medical device or borderline product imported or brought in to the country in contravention of the provisions of this Act and without obtaining an import license from the Authority; and

"veterinary surgeon" means a person registered as Veterinary Surgeon or a Veterinary Practitioner under the Veterinary Surgeons' and Practitioner Act, No. 46 of 1956.

In case of an inconsistency the Sinhala text shall prevail.

147. In the event of an inconsistency between the Sinhala and Tamil texts of this Act, the Sinhala text shall prevail.

Annual subscription of English Bills and Acts of the Parliament Rs. 885 (Local), Rs. 1,180 (Foreign), Payable to the SUPERINTENDENT, GOVERNMENT PUBLICATIONS BUREAU, DEPARTMENT OF GOVERNMENT INFORMATION, NO. 163, KIRULAPONA MAWATHA, POLHENGODA, COLOMBO 05 before 15th December each year in respect of the year following.



GUIDELINE ON REGISTRATION OF MEDICINES

OCTOBER 15, 2019

NATIONAL MEDICINE REGULATORY AUTHORITY
Norris Canal Rd, Colombo 01000, Sri Lanka

GUIDELINE ON GUIDELINES FOR REGISTRATION OF MEDICINES

CONTENTS

1. INTRODUCTION

This document "Guidelines for Registration of Medicines" will serve as the reference guide for the registration process of medicines, as defined in the NMRA Act 2015, in Sri Lanka.

This documentation shall be read in conjunction with the current laws and regulations controlling medicines in Sri Lanka. The written laws shall take precedence over this guidance document in any event of discrepancy.

The content of this Guideline shall also be read in conjunction with relevant information described in other existing World Health Organization (WHO) or International Conference on Harmonization (ICH) reference documents and guidelines.

The scope of this document includes information relating to administrative requirements and procedures for submission of an application for the registration of medicines

Applicants shall familiarize with the contents of this document and the governing legislations before they submit applications for registration of medicines.

The Authority has powers to request for information not described in this document that is deemed necessary to ensure the quality, safety, efficacy, need and price of the product.

The Authority reserves the right to amend any part of this document whenever it deems necesary.
The National Medicines Regulatory Act (NMRA Act) 2015 is the main legislation that control medicines in Sri Lanka. The Authority established under NMRA Act is tasked with ensuring the quality, safety and efficacy of medicines. The NMRA reserves the right to consider the need and the price of a medicine before granting market authorization.

As per the NMRA Act, no person shall manufacture, sell, supply, import, manufacture or advertise any medicine unless the product is a registered as a medicine with the Authority.

2. ABBREVEATIONS

API	Active Pharmaceutical Ingredient
APIMF	Active Pharmaceutical Ingredient Master File
BA	Bioavailability
BE	Bioequivalence
BCS	Biopharmaceutical Classification System
BMR	Batch Manufacturing Record
BPR	Batch Packaging Record
CEP	Certificate of Suitability
cGMP	Current Good Manufacturing Practices
CPP	Certificate of Pharmaceutical Product

CTD	Common Technical Document
DOS-PD	Dossier Overall Summary of Product Dossier
EPAR	European Public Assessment Report
FDA	Food and Drug Administration
FDC	Fixed-dose Combination
FPP	Finished Pharmaceutical Product
GMP	Good Manufacturing Practices
ICH	International Conference on Harmonisation
INN	International Non-proprietary Name
JP	Japanese Pharmacopeia
OOS	Out of Specification
OSD	Oral Solid Dosage
DP	Drug Product
PAR	Public Assessment Report
PD	Product Dossier
Ph. Eur.	European Pharmacopoeia
Ph. Int.	International Pharmacopoeia
PIL	Patient Information Leaflet
PQM	Promoting the Quality of Medicines Program
PV	Process Validation
PVC	Polyvinyl Chloride
QA	Quality Assurance
QC	Quality Control
RH	Relative Humidity
DS	Drug Substance
SMPC	Summary of Product Characteristics
SOP	Standard Operating Procedure
SRA	Stringent Regulatory Authority
UDAF	Unidirectional Air Flow
UDLAF	Unidirectional Laminar Air Flow
USAID	United States Agency for International Development
USP	U. S. Pharmacopeia
WHO	World Health Organization

3. DEFINITIONS

The following definitions are provided to facilitate interpretation of the Guideline; they apply only to the words and phrases used in this Guideline.

Active pharmaceutical ingredient (API)

Any substance or combination of substances used in a finished pharmaceutical product (FPP), intended to furnish pharmacological activity or to otherwise have direct effect in the diagnosis, cure, mitigation, treatment or prevention of disease, or to have direct effect in restoring, correcting or modifying physiological functions in human beings. Drug Substance" and "Active Substance" are synonymous to "Active Ingredient.

API starting material

A raw material, intermediate, or an API that is used in the production of an API and that is incorporated as a significant structural fragment into the structure of the API. An API starting material can be an article of commerce, a material purchased from one or more suppliers under contract or commercial agreement, or produced through in-house synthesis.

Applicant
The person or entity who submits a registration application of product to the Authority and responsible for the product information.

Batch records
All documents associated with the manufacture of a batch of bulk product or finished product. They provide a history of each batch of product and of all circumstances pertinent to the quality of the final product.

Bioavailability
The rate and relative amount of the administered drug which reaches the general circulation intact, or the rate and extent to which the API is absorbed from a drug product and becomes available at the site(s) of action.

Bioequivalence
Refer the definition given in the NMRA Act

Bio-waiver
Refer the definition given in the NMRA Act

BCS (Biopharmaceutics Classification System)
An API for which the highest dose included in the List of Essential Medicines for Sri Lanka (if the API appear in the List of Essential Medicines) or, the highest dose strength available on the market as an oral solid dosage form is soluble in 250 ml or less of aqueous media over the pH range of 1.2–6.8 at 37ºC.

Clinical trial
Any systematic study on pharmaceutical products in human subjects whether in patients or non-patient volunteers in order to discover or verify the effects of, and/or identifies any adverse reaction to investigational products, and/or to study absorption, distribution, metabolism, and excretion of the products with the object of ascertaining their efficacy and safety.

Commitment batches
Production batches of an API or finished pharmaceutical product (FPP) for which the stability studies are initiated or completed post-approval through a commitment provided with the application.

Comparator product
A pharmaceutical product with which the generic product is intended to be interchangeable in clinical practice. The comparator product will normally be the innovator product for which efficacy, safety, and quality have been established.

Dosage Form
Formulation of an active ingredient(s) so that it can be administered to a patient in specified quantity/strength, e.g., tablets, capsules, injection solution, syrups, ointments, suppositories, etc. "Pharmaceutical Form" and "Finished Product" are synonymous to "Dosage Form."

Established multisource (generic) product
A multisource product that has been marketed by the applicant or manufacturer associated with the dossier for at least five years and for which at least 10 production batches were produced over the previous year, or, if less than 10 batches were produced in the previous year, not less than 25 batches were produced in the previous three years.

Excipient
Any component of a finished dosage form other than the claimed therapeutic ingredient or active ingredients.

Finished pharmaceutical product (FPP)
A finished dosage form of a pharmaceutical product that has undergone all stages of manufacture, including packaging in its final container and labeling.

Formulation
The composition of a dosage form, including the characteristics of its raw materials and the operations required to process it.

Immediate Container
That part of a product container which is in direct contact with the drug at all times.

Innovator pharmaceutical product
Generally, the pharmaceutical product that was first authorized for marketing (normally as a patented product) on the basis of documentation of efficacy, safety, and quality.

Labeling
Includes any legend, word, or mark attached to, included in, belonging to, or accompanying any drug including: 1) the immediate container label; 2) cartons, wrappers, and similar items; 3) information materials, such as instructional brochures and package inserts.

Manufacturer
A company that carries out operations such as production, packaging, repackaging, labeling, and relabeling of products.

Marketing authorization
An official document issued for the purpose of marketing or free distribution of a product after evaluation of safety, efficacy, and quality of the product.

Master formula (MF)
A document or a set of documents specifying the starting materials, with their quantities and packaging materials, together with a description of the procedures and precautions required to produce a specified quantity of a finished product as well as the processing instructions, including in-process controls.

Multisource (generic) pharmaceutical products
Pharmaceutically equivalent or pharmaceutical alternative products that may or may not be therapeutically equivalent. Multisource pharmaceutical products that are therapeutically equivalent are interchangeable.

Officially recognized pharmacopoeia (or compendium)
Those pharmacopoeias recognized by the Authority, i.e., The International Pharmacopoeia (Ph.Int.), European Pharmacopoeia (Ph.Eur.), British Pharmacopoeia (BP), Japanese Pharmacopoeia (JP), and the United States Pharmacopeia (USP).

Ongoing stability study

The study carried out by the manufacturer on production batches according to a predetermined schedule in order to monitor, confirm, and extend the projected re-test period (or shelf-life) of the API, or to confirm or extend the shelf-life of the FPP.

Pharmaceutical equivalents
Products are pharmaceutically equivalent if they contain the same amount of the same active ingredient(s) in the same dosage form, if they meet the same or comparable standards, and if they are intended to be administered by the same route.

Pilot-scale batch
A batch of an API or FPP manufactured by a procedure fully representative of and simulating that to be applied to a full production-scale batch; for example, for solid oral dosage forms, a pilot scale is generally, at a minimum, one-tenth that of a full production scale or 100,000 tablets or capsules, whichever is the larger; unless otherwise adequately justified.

Primary batch
A batch of an API or FPP used in a stability study from which stability data are submitted in a registration application for the purpose of establishing a re-test period or shelf-life.

Production batch
A batch of an API or FPP manufactured at production scale by using production equipment in a production facility as specified in the registration dossier.

Registration
- New Registration- In the registration process when the application receives at the first time and registration granted at first time
- Renewal of Registration - In the registration process some of the medicine are issued with Provisional Registrations (PR) for a defined reason. Such medicine needs to go through the process of renewal of its registration with the submission of additional documents requested.
- Re registration - Registration of a medicine is valid for 5 years. At the end of 5 years Market Authorization Holder has to apply for registration for the continuity.

Specification
A document describing in detail the requirements with which the products or materials used or obtained during manufacture have to conform. Specifications serve as a basis for quality evaluation.

Stability
The ability of an active ingredient or a drug product to retain its properties within specified limits throughout its shelf-life. The chemical, physical, microbiological, and biopharmaceutical aspects of stability must be considered.

Starting materials for synthesis
Materials that mark the beginning of the manufacturing process as described in an application or in an APIMF. A starting material for a synthetic API is a chemical compound of defined molecular structure that contributes to the structure of the API.

Validation

The demonstration, with documentary evidence, that any procedure, process, equipment, material, activity, or system actually leads to the expected results.

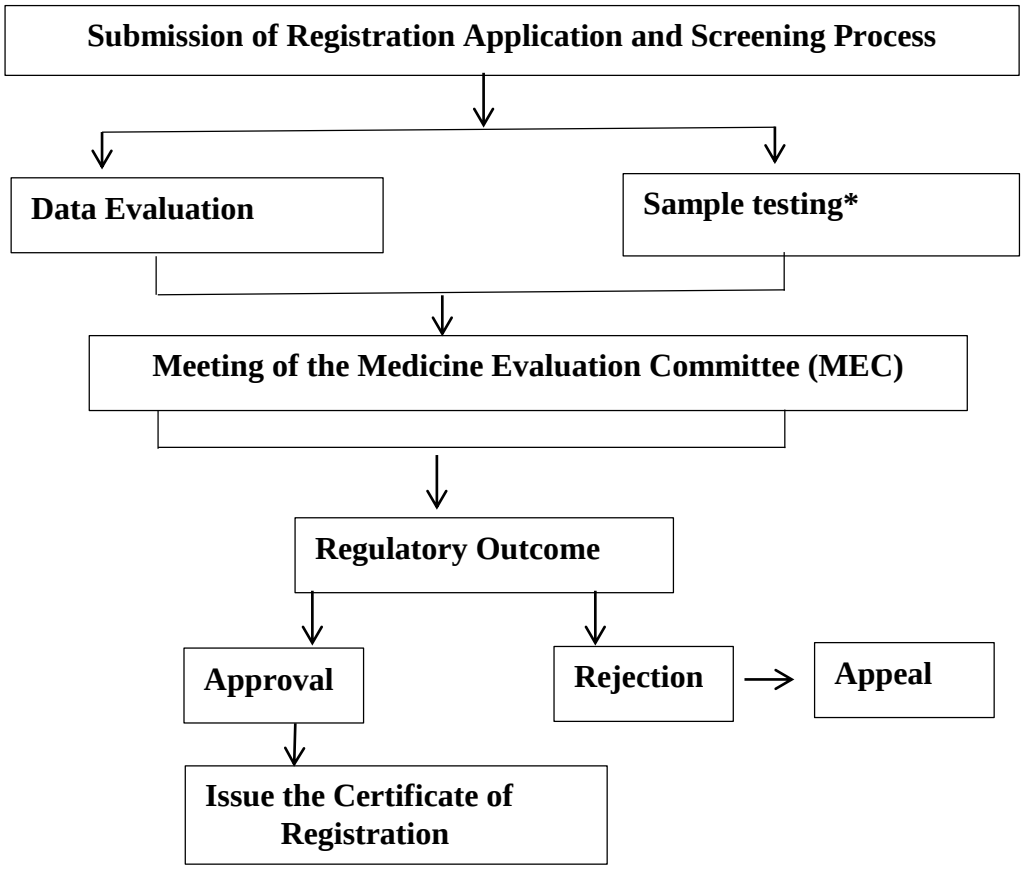
Variation

A change to any aspect of a pharmaceutical product including, but not limited to, a change to formulation, method, and site of manufacture or specifications for the finished product, ingredients, container and container labeling, and product information.

4. CATEGORIES OF APPLICATIONS FOR REGISTRATION

1. New Molecular Entities (NCE) for Sri Lanka
2. New Dosage Forms (NDF)
3. New Fixed dose Combination products
4. Biological and Biotechnological products
5. New product of existing drugs
6. Re- registration

Basic Procedure of Registration of Medicines



*for selected products

5. WHO CAN APPLY FOR REGISTRATION OF MEDICINES?

The applicant must be a locally incorporated company, corporate or legal entity, with permanent address and registered with Companies Registrar of Sri Lanka, and whose manufacturing facility has been approved for the compliance for the GMP by the NMRA.

Responsibilities of applicants

a) To ensure that all transactions with NMRA are carried by their appointed person(s);

b) Responsible for all information pertaining to quality, safety and efficacy in support of the product registration application; and shall inform the Authority in a timely manner any change in product information during course of evaluation;

Any person who knowingly supplies any false or misleading information to the Authority with his application for the registration of a product commits an offence.

c) Responsible for all matters pertaining to quality, safety and efficacy of the registered product, including:

i. Data updates on product quality, safety and efficacy or Good Manufacturing Practice (GMP) compliance of the manufacturers. Any change in any document, item, sample, particulars or information which shall be notified in writing by the applicant to the Authority within fourteen 28 calendar days from the date of such change.

ii. Any decision to withdraw the registration of the product with reasons.

d) To notify the Authority of any change in correspondence details, including the name, address, contact person, telephone number, fax number and email;

e) To notify the Authority immediately upon cessation of the applicant as the product registration holder;

6. HOW TO APPLY

- Web-based online submissions via http://www.enmra.nmra.gov.lk

7. FEES

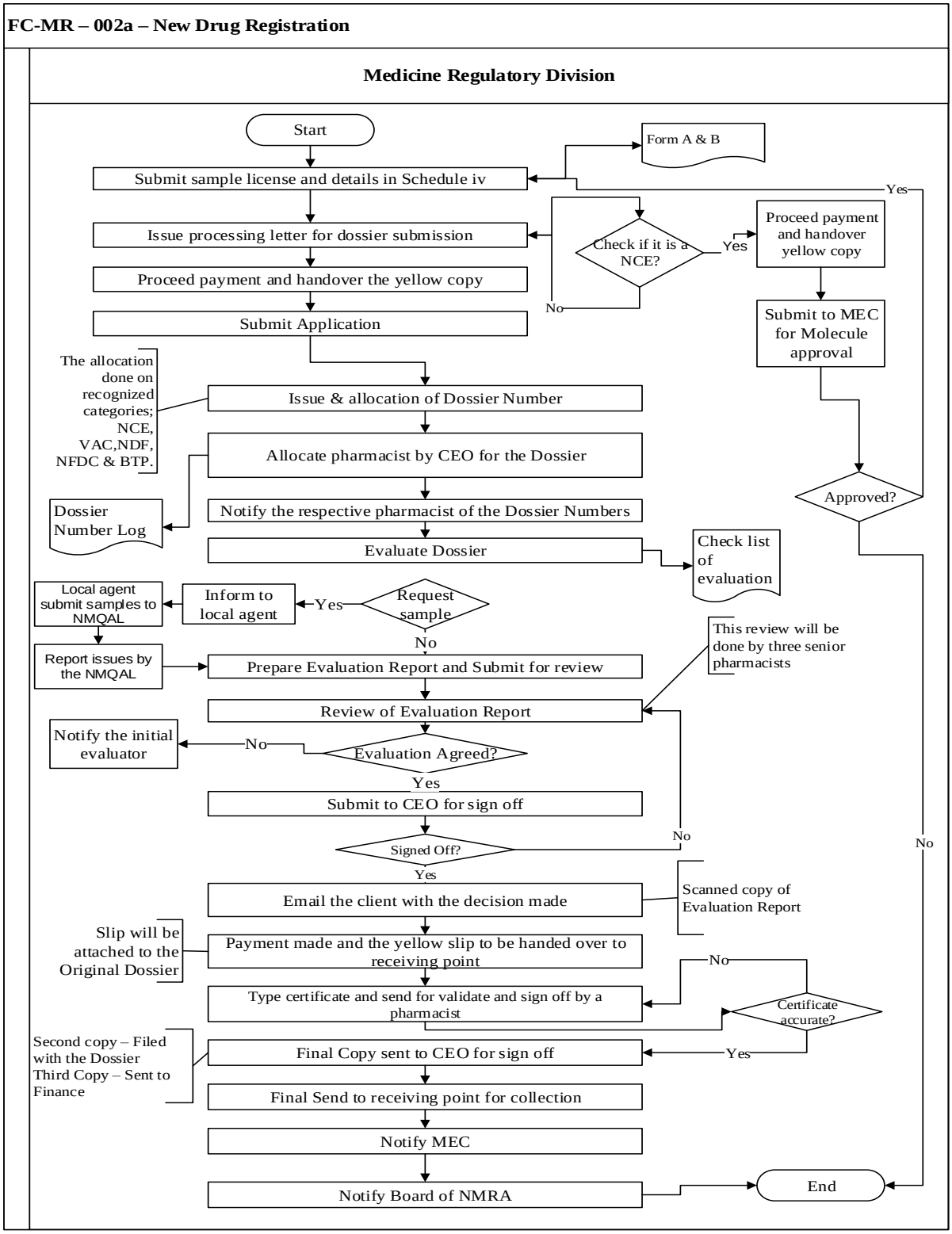
- Under the Regulation No. 2052/33, January 05, 2018 published under NMRA Act.
- The Authority may charge any applicant such costs as it may incur for the purpose of carrying out any evaluation or investigation prior to the registration of any product.
- Any payment made shall not be refundable once the application has been submitted and payment confirmed.
- Applications without the correct fees will not be processed.

8. EVALUATION AND NOTIFICATION:

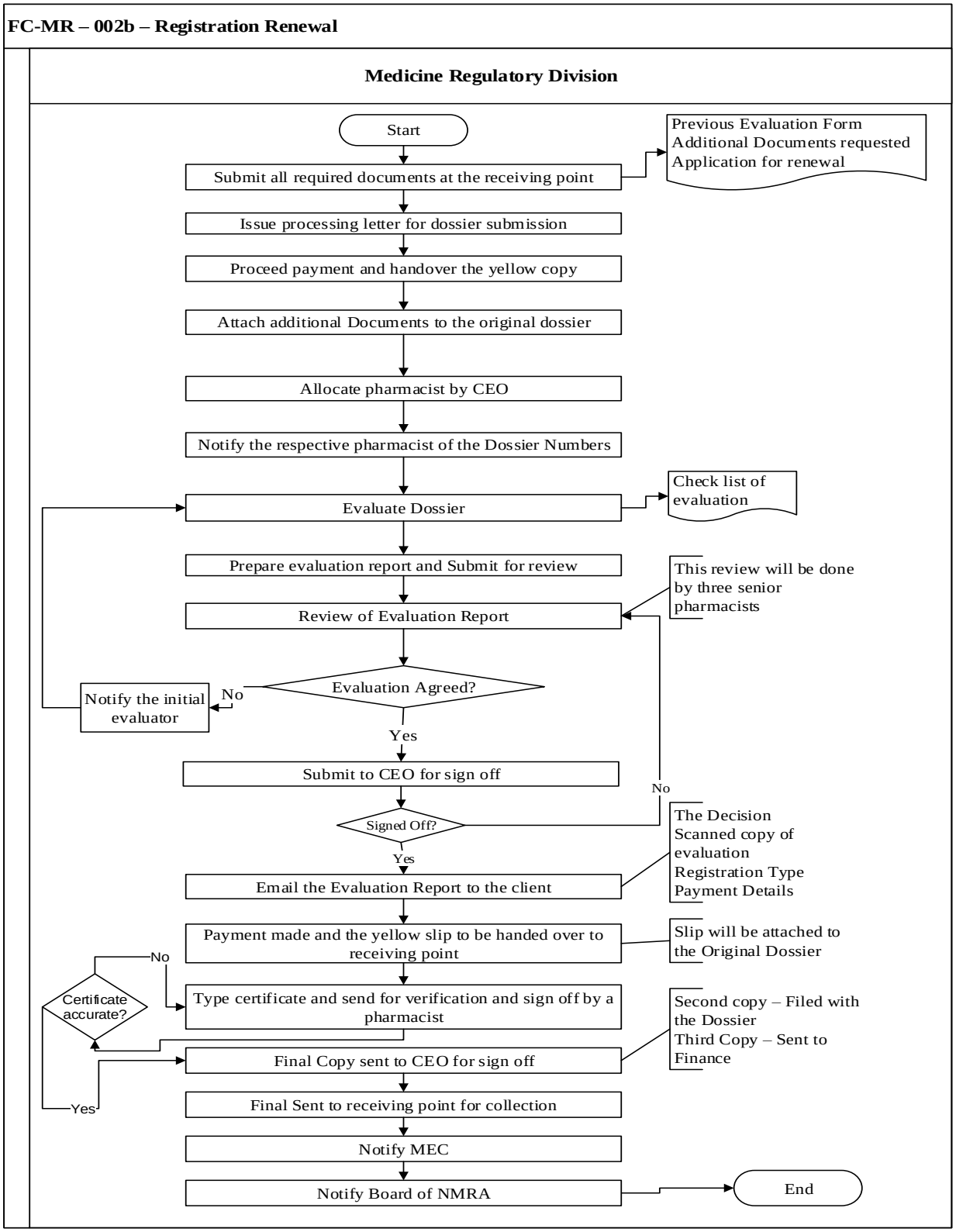
The application submitted for registration will be screened chronologically according to date of submission to the Authority, and the applicant will be notified of the results of its evaluation within 28 working days of its submission to the Authority.

9. FLOWCHARTS AND PROCEDURES

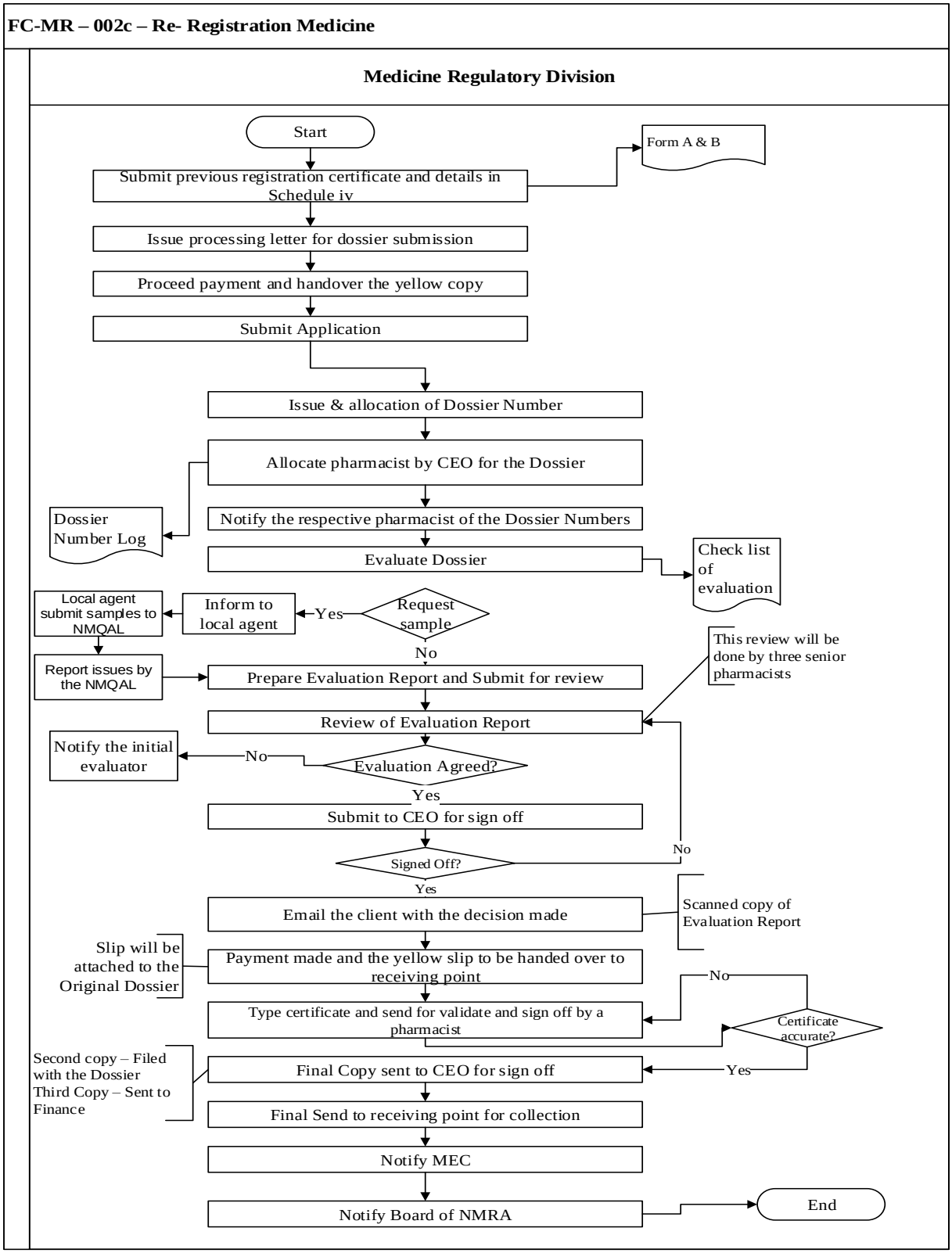
a. Submission of Dossier Procedure –New Product Registration - Flowchart



b. Registration Renewal Procedure –Flow Chart



c. Submission of Dossier Procedure – Re-Registration



10. COMPILATION OF THE DOCUMENT

The compilation of the document should be outlined according to the respective modules and should be indexed or annotated as described in this Guideline in the Common Technical Document (CTD) format.

11. THE CTD IS ORGANIZED INTO FIVE *MODULES*;

1. **Module** 1 is specific to the NMRA of Sri Lanka which includes Administrative and Product information.

Modules 2, 3, 4, and 5 are intended to be common for all situations.

2. **Module** 2 – Overviews and summaries of **Modules** 3–5;
3. **Module** 3 – Quality (pharmaceutical documentation);
4. **Module** 4: Non-clinical reports (pharmacology/toxicology);
5. **Module** 5: Clinical study reports

There may be a number of instances where repeated sections can be considered appropriate. Whenever a section is repeated, it should be made clear what the section refers to by creating a distinguishing heading, e.g., 3.2.S Drug substance (or API) (name, Manufacturer A).

12.THE FOLLOWING ARE GENERAL RECOMMENDATION FOR THE SUBMISSION OF THE DOSSIER:

- For generic products in which a molecule of an FPP is registered in Sri Lanka, Module 4 is not applicable;
- For an FPP where bioequivalence is not required, Module 4 and Module 5 are not applicable; and,
- For generic products in which a molecule of an FPP is registered in Sri Lanka and where a bioequivalence (BE) study is mandatory, only the BE study report should be provided in Module 5 of the dossier.

13. RECOMMENDATIONS FOR THE PRESENTATION OF THE INFORMATION IN THE MODULE 3 (*QUALITY MODULE)* FOR DIFFERENT SCENARIOS THAT MAY BE ENCOUNTERED:

- The Open part (non-proprietary information) of each APIMF should always be included in its entirety in the product dossier (PD), as an annex.
- For an FPP containing more than one API, one complete section should be provided for one API, followed by a complete, 3.2.S section for each additional API.

  This may not be applicable for an API where a complete listing is not possible (e.g., multivitamin)
- For an API from multiple manufacturers one complete section should be provided for the API from one manufacturer, followed by other complete sections for an additional API manufacturer;
- For an FPP with multiple strengths (e.g., 5, 15, 20mg), a separate dossier is required for each FPP;
- For an non-sterile FPP with multiple container closure systems (e.g., bottles and unit dose blisters), one complete section should be provided with information for the different presentations provided within the subsections;

- For an sterile FPP with multiple container closure systems (Ampoule, Vials and Pre-filled syringes etc), a separate dossier is required for each FPPs;
- For different dosage forms of FPPs (e.g., tablets and capsule), a separate dossier is required for each FPP;
- For an FPP supplied with reconstitution diluents (s), one complete section should be provided for the FPP, followed by the information on the diluents (s) in a separate part as appropriate;

14. GUIDANCE FOR THE APPLICANT WITH REGARD TO COMPILATION AND FOLLOW-UP OF THE PD IS LISTED HERE:

1. The application form and the Dossier Overall Summary (DOS) of the PD should always be in electronic PDF format.
2. The attached data and documents should be in the English language.
3. Paper selection: Paper size is A4. Margins for top, bottom, header, and footer are 12.5 mm, and left and right margins are 25mm.
4. Paragraph: Single line spacing.
5. Font: Minimum type size 12point.

The weight of the font should be in such a way that it text is legible when copied.

6. Any abbreviation should be clearly defined.

15. FAST TRACK REVIEW:

Fast tract review for medicines is considered in following situations;

1. Drugs used for orphan diseases, drugs considered as "orphan" to Sri Lanka by the NMRA
2. Drugs for emergency situations shall have priority for evaluation and registration.

16. PRIORITY REVIEW:

Priority Review for medicines is considered in following situation;

1. Medicines having less than 05 products registered with the NMRA.

17. VARIATIONS

In case of requests to change the contents of specifications and test methods of the product, after reviewing of the screening application, the applicant needs to follow the "Variation Guideline" published by the NMRA.

18. BRAND **(TRADE NAME):**

Brand names indicating the licensed or unlicensed indications are not accepted. Brand names inappropriate for a medicine as decided by the MEC, are also not accepted.

Appoint a technical person

The local agent or the manufacturer should appoint a technical person, a pharmacist, who is able to understand regulations and related guidelines of the Authority and registration process of products, and who can communicate with the assessors in cases of need of clarification for the queries raised by the Authority that may either be product-related or administrative issues.

Module 1 – Administrative information and prescribing information

1. Cover Letter
2. Table of Contents of the Application, including Module 1 (Modules 1-5)

3. Application Form
4. Letter of Authorization by the manufacturer
5. Certificate of Pharmaceutical product
6. Certificate of Suitability (CEP), if any
7. Product Information
    a. Summary of Product Characteristics (SPC)
    b. Labeling Information (immediate and outer label)
    c. Product information Leaflet (PI)
    d. Patient Information Leaflet (PIL) where available or requested by the NMRA

Module 2 – Dossier Overall Summary of Product Dossier

1. PD Table of Contents (Modules 2-5)
2. PD Introduction
3. Quality Overall Summary of Product Dossier
4. Nonclinical Overview – generally not applicable for multisource products (some exceptions may apply)
5. Clinical Overview
6. Nonclinical Written and Tabulated Summaries – generally not applicable for multisource products (some exceptions may apply)

Module 3 – Quality

1. Table of Contents of Module 3
2. Body of Data
3. Literature References

Module 4 – Nonclinical Study Reports – generally not applicable for multisource products(some exceptions may apply)

1. Table of Contents of Module 4
2. Study Reports
3. Literature References

Module 5 – Clinical Study Reports

1. Table of Contents of Module 5
2. Tabular Listing of all Clinical Studies
3. Clinical Study Reports
4. Reports of Biopharmaceutical Studies (mainly BE study reports for generic products
5. Case Report Forms and Individual Patient Listings – generally not applicable for multisource products(some exceptions may apply)
6. Literature References

MODULE 1: ADMINSTRATIVE AND PRODUCT INFORMATION

1.1. Covering Letter

Dated and signed letter for submission of the dossier by mentioning the product included in the dossier from the manufacturer and/or local agent responsible for registration.

1.2. Table Contents of Modules 1 to 5

Table of contents of Module 1 through Module 5 (of the PD) should be provided in Module 1.

1.3. Application Form

Completed and signed application form as provided in Annex I of this Guideline should be submitted. The date of application should correspond to the date of submission of the registration dossier to the Authority.

1.4. Agency Agreement

I. An agency agreement should be made between the manufacturer of the product for registration and the agent responsible for the import, distribution, and sale of the product in Sri Lanka.

II. Where the company manufactures the product at two or more places, the agreement and responsibility of each party made between the manufacturers should be submitted. In such a case, the agency agreement between the local agent and the manufacturer should be the site where the file is kept and the applicant for registration is registered.

III. The agreement should be signed by both parties and such is what is to be presented. The seal/stamp of both parties should also be affixed to the document for agency agreement.

IV. The appointed agent is responsible for correspondence and complete compliance with regulatory requirements pertaining to the product distribution life cycle in the country.

V. The agreement should state that if any unsuspected and unacceptable adverse event occurs to the consumer under normal utilization, all the party's (local agent, manufacturer, and/or license holder)mentioned in the agreement will be responsible for collecting the product from the market and will be responsible for substantiating any related consequences.

VI. The agreement should specify that both parties are responsible for pharmacovigilance and post-marketing reporting of the product safety, quality, and efficacy follow-up after marketing.

1.5. Certificate of a Pharmaceutical Product

- Certificate of a Pharmaceutical Product (CPP) issued by a competent authority in the exporting country should be provided in Module 1 in accordance with the format recommended by the W.H.O.
- The CPP should be valid at the time of submission, country specific and be the original.

1.6. Certificate of Suitability (CEP), if applicable

- A complete copy of the Certificate of Suitability (CEP), including any annexes, should be provided in *Module 1.* The declaration of access for the CEP should be duly filled out by the CEP holder on behalf of the FPP manufacturer or applicant to the Authority.
- In addition, a written commitment should be included that states the applicant will inform the Authority in the event that the CEP is withdrawn. It should also be acknowledged by the applicant

that withdrawal of the CEP will require additional consideration of the API data requirements to support the PD. The written commitment should accompany the copy of the CEP in Module 1.

- Along with the CEP, the applicant should supply the following information in the dossier, with data summarized in the PD and Module 3 of the dossier:

I. *General properties* – discussion of any additional applicable physicochemical and other relevant API properties that are not controlled by the CEP and Ph.Eur. monograph, e.g. solubility and polymorphs.

II. *Elucidation of structure and other characteristics*– studies to identify polymorphs (exception: where the CEP specifies a polymorphic form) and particle size distribution, where applicable.

III. *Specification* – the specifications of the FPP manufacturer, including all tests and limits of the CEP and Ph.Eur. monograph, and any additional tests and acceptance criteria that are not controlled in the CEP and Ph.Eur. monograph, such as polymorphs and/or particle size distribution.

IV. *Analytical procedures and validation* – for any tests in addition to those in the CEP and Ph.Eur. monograph.

V. *Batch analysis*– results from three batches of at least one pilot scale, demonstrating compliance with the FPP manufacturer's API specifications.

VI. *Container closure system*– specifications including descriptions and identification of primary packaging components(exception: where the CEP specifies a re-test period).

1.7. Product information

- Product information including package insert (s), labeling, and summary of product characteristics (SmPC) should be provided in Module 1 of the dossier.
- All product information label statements are required to be in English. Any information appearing in the product information (labels, PIL, and SmPC) should be based on scientific justification.

1.7.1. Summary of Product Characteristics

- Recommended format for the content of the SPC is provided in Annex 3 of this Guideline.

1.7.2. Labeling (immediate and outer label)

- Only original labels or computer-ready color-printed labels (art work) are accepted for final approval.
- In the case where the text of the labels is printed directly on plastic bottles through a silk screen process, photocopies of these labels will be accepted for approval.
- The titles for batch number, manufacturing, and expiry dates should be part of the printing. If the labeling technology of the manufacturer is such that this information is to be printed on the label during production, a written commitment to show all the required information on the label of the finished product must be submitted.
- The contents of the label are given in "Guidelines for labeling" published by NMRA.

1.7.3. Product Information Leaflet (PI)

- The general content of the PIL should be prepared in line with the content of the SPC.
- Recommended format for the content of the SPC is provided in Annex 3 of this Guideline

- The contents of the PI are given in "Guidelines for labeling" published by NMRA.

1.7.4 Patient Information Leaflet (PIL)

- The general content of the PIL should be prepared in line with the content of the SPC. The PIL should not be described or presented in a manner that is false, misleading, or deceptive or is likely to create an erroneous impression regarding its use in any respect, either pictorially or in words.
- The medicines for which a PIL is a requirement and the contents of the PIL are given in "Guidelines for labeling" published by NMRA.

MODULE 2: DOSSIER OVERALL SUMMARY (DOS)

The Dossier Overall Summary (DOS) is a summary that follows the scope and the outline of the body of data provided in Module 3, Module 4 and Module 5.

- The DOS should not include information, data, or justification that was not already included in Module 3, Module 4, and Module 5 or in other parts of the dossier.
- The DOS should include sufficient information from each section to provide the assessors with an overview of the PD.
- The DOS should also emphasize critical key parameters of the product and provide, for instance, justification in cases where guidelines were not followed.
- The DOS should include a discussion of key issues that integrates information from sections in the Safety, Efficacy, and Quality Module and supporting information from other modules (e.g., qualification of impurities via toxicological studies), including cross-referencing to volume and page number in other Modules.
- The use of tables to summarize the information is encouraged, where possible. Other approaches to summarize the information can be used if they fulfil the same purpose.

MODULE 3: QUALITY

3.1. BODY OF DATA

3.1.S Drug Substance 1 (Name, Manufacturer)

3.1.S.1 General Information (Name, Manufacturer)

3.1.S.1.1 Nomenclature (name, manufacturer)

Information on the nomenclature of the drug substance should be provided. For example:

1. Recommended International Non-proprietary Name (INN);
2. Pharmacopoeia name, if relevant;
3. Chemical name(s);
4. Other non-proprietary name(s) (e.g., national name, United States Adopted Name(USAN), Japanese Accepted Name (JAN), British Approved Name (BAN)) and Chemical Abstracts Service (CAS) registry number.

*A **CAS Registry Number**, also referred to as CASRN or **CAS Number**, is a unique numerical identifier assigned by the **Chemical Abstracts Service (CAS)** to every **chemical** substance described in the open scientific literature.*

5. Anatomical Therapeutic Chemical (ATC) Class

*The Anatomical Therapeutic Chemical (ATC) Classification System is a drug classification system that classifies the **active** ingredients of drugs according to the organ or system on which they act and their therapeutic, **pharmacological** and chemical properties.*

The listed chemical names should be consistent with those appearing in scientific literature and those appearing on the product labeling information (e.g., summary of product characteristics; package leaflet, also known as patient information leaflet or PIL; or labeling). Where several names exist, the INN name should be indicated.

3.1.S.1.2 Structure (name, manufacturer)

- The structural formula, including relative and absolute stereochemistry, the molecular formula, and the relative molecular mass should be provided.
- For bio-tech drug substance, the schematic amino acid sequence indicating glycosylation sites or other post-translational modifications and relative molecular mass should be provided, as appropriate.

3.1.S.1.3 General properties (name, manufacturer)

- A list should be provided of physicochemical and other relevant properties of the drug substance, including biological activity for Biotech. (Reference: ICH Guidelines Q6A and Q6B). This information can be used in developing the specifications, in formulating FPPs, and in testing for release and stability purposes.
- The physical and chemical properties of the API should be discussed, including the physical description, solubility in common solvents (e.g., water, alcohols, dichloromethane, acetone), quantitative aqueous pH solubility profile (e.g., pH 1.2 to 6.8, dose/solubility volume), polymorphism, pH and pKa values, UV absorption maxima and molar absorptivity, melting point, refractive index (for a liquid), hygrocopicity, partition coefficient, etc. This list is not intended to be exhaustive, but provides an indication as to the type of information that could be included.

3.1. S.2 Manufacture (Name, Manufacturer)

3.1. S.2.1 Manufacturer(s) (name, manufacturer)

- The name, address, and responsibility of each manufacturer, including contractors, and each proposed production site or facility involved in manufacturing and testing should be provided.
- The list of manufacturers/companies should specify the actual addresses of production or manufacturing site(s) involved (including block(s) and units(s)), rather than the administrative offices. Telephone number(s), fax number(s) and e-mail address(es) should be provided.
- A valid manufacturing authorization should be provided for the production of APIs. If available, a certificate of GMP compliance should be provided in the PD in Module 1.

3.1.S.2.2 Description of manufacturing process and process controls (name, manufacturer)

- The description of the drug substance manufacturing process represents the applicant's commitment for the manufacture of the drug substance. Information should be provided to adequately describe the manufacturing process and process controls.
- For a synthetic drug substance, a flow diagram of the synthetic process(es) should be provided that includes molecular formulae, weights, yield ranges, chemical structures of starting materials,

intermediates, reagents and API reflecting stereochemistry, and identifies operating conditions and solvents.

- Where possible, and for confidentiality reasons, the holder of the APIMF can submit the restricted part of the APIMF to the Authority. In this case, if detailed information is presented in the restricted part, the information to be provided for this section of the applicant FPP PD includes a flow chart (including molecular structures and all reagents and solvents) and a brief outline of the manufacturing process, with special emphasis on the final steps, including purification procedures.
- For sterile APIs, full validation data on the sterilization process should be provided in the Open part (in cases where there is no further sterilization of the final product).
- For biotech drug substance, information should be provided on the manufacturing process, which typically starts with a vial(s) of the cell bank, and includes cell culture, harvest(s), purification and modification reactions, filling, storage, and shipping conditions. An explanation of the batch numbering system, including information regarding any pooling of harvests or intermediates and batch size or scale should be provided.
- A flow diagram should be provided that illustrates the manufacturing route from the original inoculum (e.g., cells contained in one or more vials(s) of the Working Cell Bank up to the last harvesting operation. The diagram should include all steps (i.e., unit operations) and intermediates. Relevant information for each stage, such as population doubling levels, cell concentration, volumes, pH, cultivation times, holding times, and temperature, should be included. Critical steps and critical intermediates for which specifications are established (as mentioned in 3.1.S.2.4) should be identified.
- A description of each process step in the flow diagram should be provided. Information should be included on, for example, scale; culture media and other additives (details provided in 3.1.S.2.3); major equipment (details provided in 3.1.A.1); and process controls, including in-process tests and operational parameters, process steps, equipment and intermediates with acceptance criteria (details provided in 3.1.S.2.4).
- Where polymorphic/amorphous forms have been identified, the form resulting from the synthesis should be stated. Where particle size is considered a critical attribute, the particle size reduction method(s) (milling, micronization) should be described.
- Where there are multiple manufacturing sites for one API manufacturer, a comprehensive list, in tabular form, should be provided comparing the processes at each site and highlighting any differences.

3.1. S.2.3 Control of materials (name, manufacturer)

- Materials used in the manufacture of the drug substance (e.g., raw materials, starting materials, solvents, reagents, catalysts) should be listed identifying where each material is used in the process. Information on the quality and control of these materials should be provided.
- Information demonstrating that materials (including biologically-sourced materials, e.g., media components, monoclonal antibodies, enzymes) meet standards appropriate for their intended use (including the clearance or control of adventitious agents) should be provided, as appropriate. For biologically-sourced materials, this can include information regarding the source, manufacture, and characterization.
- The carry-over of impurities of the starting materials for synthesis into the final API should be considered and discussed.

- A letter of attestation should be provided confirming that the API and the starting materials and reagents used to manufacture the API are *without* risk of transmitting agents of animal spongiform encephalopathies. When available, a CEP demonstrating Transmissible Spongiform Encephalopathy (TSE)-compliance should be provided. A complete copy of the CEP (including any annexes) should be provided in Module 1.

3.1. S.2.4 Controls of critical steps and intermediates (name, manufacturer)

Critical Steps:

- Tests and acceptance criteria (with justification including experimental data) performed at critical steps identified in 3.1.S.2.2 of the manufacturing process to ensure that the process is controlled should be provided.

Intermediates:

- Information on the quality and control of intermediates isolated during the process should be provided. Specifications for isolated intermediates should be provided and should include tests and acceptance criteria for identity, purity and assay, where applicable

Additionally for Biotech: Stability data supporting storage conditions should be provided. (Reference: ICH Guideline Q5C)

3.1. S.2.5 Process validation and/or evaluation (name, manufacturer)

- It is expected that the manufacturing processes for all APIs are properly controlled. If the API is prepared as sterile, a complete description should be provided for aseptic processing and/or sterilization methods. The controls used to maintain the sterility of the API during storage and transportation should also be provided.
- For biotech drug substances, sufficient information should be provided on validation and evaluation studies to demonstrate that the manufacturing process (including reprocessing steps) is suitable for its intended purpose and to substantiate selection of critical process controls (operational parameters and in-process tests) and their limits for critical manufacturing steps (e.g., cell culture, harvesting, purification, and modification).
- The plan for conducting the study should be described and the results, analysis and conclusions from the executed study should be provided. The analytical procedures and corresponding validation should be cross-referenced (e.g., 3.1.S.2.4, 3.1.S.4.3) or provided as part of justifying the selection of critical process controls and acceptance criteria.
- For manufacturing steps intended to remove or inactivate viral contaminants, the information from evaluation studies should be provided in 3.1.A.2.

3.1.S.2.6 Manufacturing process development (name, manufacturer)

- A description and discussion should be provided of the significant changes made to the manufacturing process and/or manufacturing site of the API used in producing comparative bioavailability or bio-waiver, scale-up, pilot, clinical and, if available, production scale batches.
- Testing used to assess the impact of manufacturing changes on the drug substance(s)and the corresponding drug product(s) can also include nonclinical and clinical studies. Cross-reference to the location of these studies in other modules of the submission should be included

3.1.S.3 Characterization (Name, Manufacturer)

3.1.S.3.1 Elucidation of structure and other characteristics (name, manufacturer)

- Confirmation of structure based on, e.g., synthetic route and spectral analyses should be provided. Information such as the potential for isomerism, the identification of stereochemistry, or the potential for forming polymorphs should also be included.
- For biotech drug substance for the desired product and product-related substances, details should be provided on primary, secondary, and higher-order structure, post-translational forms (e.g., glycoforms), biological activity, purity, and immunochemical properties, when relevant. [Reference: ICH Guideline Q6B]

Elucidation of structure

- The PD should include quality assurance (QA)-certified copies of the spectra, peak assignments, and a detailed interpretation of the data of the studies performed to elucidate and/or confirm the structure of the API. The DOS-PD should include a list of the studies performed and a conclusion from the studies that the results support the proposed structure.
- For APIs that are not described in an officially recognized pharmacopoeia, the studies carried out to elucidate and/or confirm the chemical structure normally include elemental analysis, infrared (IR), ultraviolet (UV), nuclear magnetic resonance (NMR), and mass spectra (MS) studies. Other tests could include X-ray powder diffraction (XRPD) and differential scanning calorimetry (DSC).
- For APIs that are described in an officially recognized pharmacopoeia, it is generally sufficient to provide copies of the IR spectrum of the API from each of the proposed manufacturer(s) runs concomitantly with a pharmacopoeial reference standard. See Section 3.1.S.5 for details on acceptable reference standards or materials.

Isomerism/stereochemistry

- When an API is chiral, it should be specified whether specific stereoisomers or a mixture of stereoisomers have been used in the clinical or the comparative bio-studies, and information should be given as to the stereoisomer of the API that is to be used in the FPP.

Polymorphism

- Many APIs can exist in different physical forms in the solid state. Polymorphism is characterized as the ability of an API to exist as two or more crystalline phases that have different arrangements and/or conformations of the molecules in the crystal lattice. Amorphous solids consist of disordered arrangements of molecules and do not possess a distinguishable crystal lattice. Solvates are crystal forms containing either stoichiometric or nonstoichiometric amounts of a solvent. If the incorporated solvent is water, the solvates are also commonly known as hydrates.
- Polymorphic forms of the same chemical compound differ in internal solid-state structure and, therefore, may possess different chemical and physical properties, including packing, thermodynamic, spectroscopic, kinetic, interfacial, and mechanical properties. These properties can have a direct impact on API process-ability, pharmaceutical product manufacturability, and product quality/performance, including stability, dissolution and bioavailability. Unexpected appearance or disappearance of a polymorphic form may lead to serious pharmaceutical consequences.

3.1.S.3.2 Impurities (name, manufacturer)

- Information on impurities should be provided. [Reference: ICH Guidelines Q3A, Q3C, Q5C, Q6A, and Q6B]
- Regardless of whether a pharmacopoeial standard is claimed, a discussion should be provided of the potential and actual impurities arising from the synthesis, manufacture, or degradation of the API. This should cover starting materials, by-products, intermediates, chiral impurities, and degradation products and should include the chemical names, structures, and origins. The discussion of pharmacopoeial APIs should not be limited to the impurities specified in the API monograph.

Identification threshold

- It is recognized by the pharmacopoeias that APIs can be obtained from various sources and thus can contain impurities not considered during the development of the monograph. Furthermore, a change in the production or source may give rise to additional impurities that are not adequately controlled by the official pharmacopoeia monograph. As a result, each PD is assessed independently to consider the potential impurities that may arise from the proposed route(s) of synthesis. For these reasons, the ICH limits for unspecified
- impurities (e.g., NMT 0.10% or 1.0 mg per day intake (whichever is lower) for APIs having a maximum daily dose of ≤2 g/day) are generally recommended, rather than the general limits for unspecified impurities that may appear in the official pharmacopoeia monograph that could potentially be higher than the applicable ICH limit.

Qualification of impurities

- The ICH impurity guidelines should be consulted for options on the qualification of impurities. The limit specified for an identified impurity in an *officially recognized pharmacopoeia* is generally considered to be qualified. The following is an additional option for qualification of impurities in existing APIs:
- The limit for an impurity present in an existing API can be accepted by comparing the impurity results found in the existing API with those observed in an innovator product using the same validated, stability-indicating analytical procedure (e.g., comparative high performance liquid chromatography (HPLC) studies). If samples of the innovator product are not available, the impurity profile may also be compared to a different comparator (market leading) FPP with the same route of administration and similar characteristics (e.g., tablet versus capsule). It is recommended that the studies be conducted on comparable samples (e.g., age of samples) to obtain a meaningful comparison of the impurity profiles.
- Levels of impurities generated from studies under accelerated or stressed storage conditions of the innovator or comparator FPP are not considered acceptable/qualified.
- A specified impurity present in the existing API is considered qualified if the amount of the impurity in the existing API reflects the levels observed in the innovator or comparator (market leading) FPP.
- ICH class II solvent(s) used prior to the last step of the manufacturing process may be exempted from routine control in API specifications if suitable justification is provided. Submission of results demonstrating less than 10% of the ICH Q3C limit (option I) of the solvent(s) in three consecutive production-scale batches or six consecutive pilot-scale batches of the API or a suitable intermediate would be considered acceptable justification. The last-step solvents used in the process should always be routinely controlled in the final API. The limit for residues of triethylamine (TEA) is either 320 ppm on the basis of ICH Q3C (option 1) or 3.2 mg/day on the basis of permitted daily exposure (PDE).

- The absence of known, established, highly toxic impurities (genotoxic) used in the process or formed as a by-product should be discussed and suitable limits should be proposed. The limits should be justified by appropriate reference to available guidance's (e.g., EMEA/CHMP/QWP/251344/2006 or USFDA Guidance for Industry: Genotoxic and carcinogenic impurities in drug substances and products, recommended approaches,
- Residues of metal catalysts used in the manufacturing process and determined to be present in batches of API are to be controlled in specifications. This requirement does not apply to metals that are deliberate components of the pharmaceutical substance (such as a counter ion of a salt) or metals that are used as a pharmaceutical excipient in the FPP (e.g., an iron oxide pigment). The guideline on the specification limits for residues of metal catalysts or metal reagents, EMEA/CHMP/SWP/4446/2000, or any equivalent approaches can be used to address this issue. The requirement normally does not apply to extraneous metal contaminants that are more appropriately addressed by GMP, WHO Good Distribution Practices for Pharmaceutical Products (GDP), or any other relevant quality provision such as the heavy metal test in monographs of recognized pharmacopoeias that cover metal contamination originating from manufacturing equipment and the environment.

3.1.S.4 Control of Drug Substance (name, manufacturer)

3.1.S.4.1 Specification (name, manufacturer)

- The specification for the drug substance should be provided. Copies of the API specifications, dated and signed by authorized personnel (e.g., the person in charge of the quality control or quality assurance department) should be provided in the PD, including specifications from each API manufacturer as well as those of the FPP manufacturer.
- The FPP manufacturer's API specification should be summarized according to the table in the DOS-PD template under the headings tests, acceptance criteria, and analytical procedures (including types, sources, and versions for the methods).
- The s*tandard* declared by the applicant could be an officially recognized pharmacopoeia standard (e.g.,Ph.Int.,Ph.Eur., BP, USP, JP) or a House (manufacturer's) standard.
- The *specification reference number and version* (e.g., revision number and/or date) should be provided for version control purposes.
- For the analytical procedures, the *type* should indicate the kind of analytical procedure used (e.g., visual, IR, UV, HPLC, laser diffraction); the *source* refers to the origin of the analytical procedure (e.g., Ph.Int.,Ph.Eur., BP, USP, JP, in-house); and the *version* (e.g., code number/version/date) should be provided for version control purposes.
- In cases where there is more than one API manufacturer, the FPP manufacturer's API specifications should be one single compiled set of specifications that is identical for each manufacturer. It is acceptable to lay down in the specification more than one acceptance criterion and/or analytical method for a single parameter with the statement ―for API from manufacturer A‖ (e.g., in the case of residual solvents).
- Any non-routine testing should be clearly identified as such and justified along with the proposal on the frequency of non-routine testing.
- The ICH Q6A guideline outlines recommendations for a number of *universal* and *specific tests* and criteria for APIs. [Reference: ICH Guidelines Q3A, Q3C, Q6A; officially recognized pharmacopoeia]

3.1.S.4.2 Analytical procedures (name, manufacturer)

- The analytical procedures used for testing the drug substance should be provided. Copies of the in-house analytical procedures used to generate testing results provided in the PD, as well as those proposed for routine testing of the API by the FPP manufacturer should be provided. Unless modified, it is not necessary to provide copies of officially recognized pharmacopoeia analytical procedures.
- The system suitability tests (SSTs) represent an integral part of the method and are used to ensure the adequate performance of the chosen chromatographic system. As a minimum, HPLC and GC purity methods should include SSTs for resolution and repeatability. For HPLC methods to control API-related impurities, this is typically done using a solution of the API with a concentration corresponding to the limit for unspecified impurities. Resolution of the two closest eluting peaks is generally recommended. However, the choice of alternate peaks can be used if justified (e.g., choice of a toxic impurity).The method for repeatability test should include an acceptable number of replicate injections. HPLC assay methods should include SSTs for repeatability and in addition either peak asymmetry, theoretical plates or resolution. For thin layer chromatography (TLC) methods, the SSTs should verify the ability of the system to separate and detect the analyte(s) (e.g., by applying a spot corresponding to the API at a concentration corresponding to the limit of unspecified impurities). [Reference: ICH Guideline Q2; WHO Technical Report Series, No. 943, Annex 3]

3.1.S.4.3 Validation of analytical procedures (name, manufacturer)

- Analytical validation information, including experimental data for the analytical procedures used for testing the drug substance, should be provided.
- Copies of the validation reports for the analytical procedures used to generate testing results, as well as those proposed for routine testing of the API by the FPP manufacturer should be provided.
- In general, verification is not necessary for pharmacopoeia API *assay* methods. However, specificity of a specific pharmacopoeia assay method should be demonstrated if there are any potential impurities that are not specified in the pharmacopoeia monograph. If an officially recognized pharmacopoeia method is used to control API-related impurities that are not specified in the monograph, full validation of the method is expected with respect to those impurities.
- If an officially recognized pharmacopoeia standard is claimed and an in-house method is used in lieu of the pharmacopoeia method (e.g., for assay or for specified impurities), equivalency of the in-house and pharmacopoeia methods should be demonstrated. This could be accomplished by performing duplicate analyses of one sample by both methods and providing the results from the study. For impurity methods, the sample analyzed should be the API spiked with impurities at concentrations equivalent to their specification limits.

3.1.S.4.4 Batch analyses (name, manufacturer)

- Description of batches and results of batch analyses should be provided. The information provided should include batch number, batch size, date and production site of relevant API batches used in comparative bioavailability or biowaiver studies, preclinical and clinical data (if relevant), stability, pilot, scale-up and, if available, production-scale batches. This data is used to establish the specifications and evaluate consistency in API quality.

- Analytical results should be provided from at least two batches of, at least, pilot-scale from each proposed manufacturing site of the API and should include the batch(es) used in the comparative bioavailability or biowaiver studies. A pilot-scale batch should be manufactured by a procedure fully representative of and simulating that to be applied to a full production-scale batch.
- Copies of the certificates of analysis, both from the API manufacturer(s) and the FPP manufacturer, should be provided for the profiled batches and any company responsible for generating the test results should be identified. The FPP manufacturer's test results should be summarized in the DOS-PD.
- The discussion of results should focus on observations noted for the various tests, rather than reporting comments such as ―all tests meet specifications.‖ For quantitative tests (e.g., individual and total impurity tests and assay tests), it should be ensured that actual *numerical results* are provided rather than vague statements such as ―within limits‖ or ―conforms.‖
- A discussion and justification should be provided for any incomplete analyses (e.g., results not tested according to the proposed specification).

3.1.S.4.5 Justification of specification (name, manufacturer)

- Justification for the drug substance specification should be provided.
- A discussion should be provided on the inclusion of certain tests, evolution of tests, analytical procedures and acceptance criteria, differences from the officially recognized pharmacopoeia standard(s), etc. If the officially recognized pharmacopoeia methods have been modified or replaced, a discussion should be included.
- The justification for certain tests, analytical procedures and acceptance criteria may have been discussed in other sections of the PD (e.g., impurities, particle size distribution) and does not need to be repeated here, although a cross-reference to their location should be provided. [Reference: ICH Guidelines Q3A, Q3C, Q6A; *officially recognized pharmacopoeia]*

3.1.S.5 Reference Standards or Materials (Name, Manufacturer)

- Information should be provided on the reference standard(s) used to generate data in the PD, as well as those to be used by the FPP manufacturer in routine API and FPP testing.
- The source(s) of the reference standards or materials used in the testing of the API should be provided (e.g., those used for the identification, purity, assay tests). These could be classified as *primary* or *secondary* reference standards.
- A secondary (or in-house) reference standard can be used by establishing it against a suitable primary reference standard, e.g., by providing legible copies of the IR of the primary and secondary reference standards run concomitantly and by providing its certificate of analysis, including assay determined against the primary reference standard. [Reference: ICH Guideline Q6A; WHO Technical Report Series, No. 943, Annex 3]

3.1.S.6 Container Closure System (Name, Manufacturer)

- A description of the container closure system(s) should be provided, including the identity of materials of construction of each primary packaging component, and their specifications. The specifications should include description and identification (and critical dimensions with drawings, where appropriate). Non-pharmacopoeia methods (with validation) should be included, where appropriate.

- Copies of the labels applied on the secondary packaging of the API should be provided and should include the conditions of storage. In addition, the name and address of the manufacturer of the API should be stated on the container, regardless of whether relabeling is conducted at any stage during the API distribution process.

3.1.S.7 Stability (Name, Manufacturer)

3.1.S.7.1 Stability summary and conclusions (name, manufacturer)

- The types of studies conducted, protocols used, and the results of the studies should be summarized. The summary should include results, for example, from forced degradation studies and stress conditions, as well as conclusions with respect to storage conditions and re-test date or shelf-life, as appropriate.

Stress testing

- As outlined in the ICH Q1A guidance document, stress testing of the API can help identify the likely degradation products, which can in turn help establish the degradation pathways and the intrinsic stability of the molecule and validate the stability indicating power of the analytical procedures used. The nature of the stress testing will depend on the individual API and the type of FPP involved.
- Stress testing may be carried out on a single batch of the API. For examples of typical stress conditions, refer to WHO Technical Report Series, No. 953, Annex 2, Section 2.1.2, as well as, ―A typical set of studies of the degradation paths of an active pharmaceutical ingredient, in WHO Technical Report Series, No. 929, Annex 5, Table A.1.
- When available, it is acceptable to provide the relevant data published in the scientific literature (inter alia WHOPARs, EPARs) to support the identified degradation products and pathways.

Accelerated and long-term testing

- Available information on the stability of the API under accelerated and long-term conditions should be provided, including information in the public domain or obtained from scientific literature. The source of the information should be identified.
- The preferred long-term storage conditions for APIs is either 30ºC±2ºC/65%±5%RH or 30ºC±2ºC/75%±5%RH.Alternative conditions should be supported with appropriate evidence, which may include literature references or in-house studies, demonstrating that storage at 30ºC is inappropriate for the API. For APIs intended for storage in a refrigerator and those intended for storage in a freezer refer to the stability guideline, WHO Technical Report Series, No. 953 Annex 2. APIs intended for storage below -20°C should be treated on a case-by-case basis.
- To establish the re-test period, data should be provided on not less than three batches of, at least, pilot-scale. The batches should be manufactured by the same synthesis route as production batches and using a method of manufacture and procedure that simulates the final process to be used for production batches. The stability testing program and results should be summarized in the dossier and in the tables in the PD.
- The information on the stability studies should include details such as storage conditions, batch number, batch size, container closure system, and completed (and proposed) test intervals. The discussion of results should focus on observations noted for the various tests, rather than reporting comments such as all tests meet specifications.

- Ranges of analytical results where relevant and any trends that were observed should be included. For quantitative tests (e.g., individual and total degradation product tests and assay tests), it should be ensured that actual numerical results are provided rather than vague statements, such as "within limits" or "conforms".
- Where different from the methods described in S.4.2, descriptions and validation of the methodology used in stability studies should be provided.
- The data required at the time of submitting the dossier (in general) are:

Storage temperature (°C)	**Relative humidity (%)**	**Minimum time period (months)**
Accelerated 40±2	75±5	6
Intermediate *	*	*
Long-term 30±2	75±5	6

Ongoing stability studies

- The stability of the API should be monitored according to a continuous and appropriate program that will permit the detection of any stability issue (e.g., changes in levels of degradation products).The purpose of the ongoing stability program is to monitor the API and to determine that the API remains and can be expected to remain within the re-test period in all future batches.
- At least one production batch per year of API (unless none is produced during that year) should be added to the stability monitoring program and tested at least annually to confirm the stability. In certain situations, additional batches should be included. A written commitment (signed and dated) from API manufacturer for ongoing stability studies should be included in the dossier.
- Refer to WHO Technical Report Series, No. 953, Annex 2, Section 2.1.11, for further information on ongoing stability studies.

3.1.S.7.3 Stability data (name, manufacturer)

- The actual stability results used to support the proposed re-test period should be included in the dossier. The result should be presented in an appropriate format such as tabular, graphical, or narrative description. Information on the analytical procedures used to generate the data and validation of these procedures should be included. For quantitative tests (e.g., individual and total degradation product tests and assay tests), it should be ensured that actual numerical results are provided rather than vague statements such as ―within limits‖ or ―conforms.‖[Reference: ICH Guidelines Q1A, Q1B, Q1D, Q1E, Q2; WHO Technical Report Series, No. 953, Annex 2]

3.2. P Drug Product (Finished Pharmaceutical Product (FPP))

3.1.P.1 Description and Composition of the FPP (Name, Dosage Form)

A description of the FPP and its composition should be provided. The information provided should include, for example:

Description of the dosage form

- The description of the FPP should include the physical description, available strengths, release mechanism (e.g., immediate, modified (delayed or extended)), as well as any other distinguishable characteristics.

Composition of the dosage form

- Composition of the dosage form, and their amounts on a per unit basis (including overages, if any), the function of the components, and a reference to their quality standards (e.g., pharmacopoeia monographs or manufacturer's specifications) should be provided.
- All components used in the manufacturing process should be included, including those that may not be added to every batch (e.g., acid and alkali), those that may be removed during processing (e.g., solvents), and any others (e.g., nitrogen, silicon for stoppers).
- If the FPP is formulated using an active moiety, then the composition for the active ingredient should be clearly indicated (e.g.,1 mg of active ingredient base=1.075 mg active ingredient hydrochloride).
- All overages should be clearly indicated (e.g., contains 2% overage of the API to compensate for manufacturing losses).
- The components should be declared by their proper or common names, quality standards (e.g., Ph.Int., Ph.Eur., BP, USP, JP, House) and, if applicable, their grades (e.g., Microcrystalline Cellulose NF (PH 102)) and special technical characteristics (e.g., lyophilized, micronized, solubilized, emulsified).
- The function of each component (e.g., diluent/filler, binder, disintegrant, lubricant, glidant, granulating solvent, coating agent, antimicrobial preservative) should be stated. If an excipient performs multiple functions, the predominant function should be indicated.
- The qualitative composition, including solvents, should be provided for all proprietary components or blends (e.g., capsule shells, coloring blends, imprinting inks). This information (excluding the solvents) is to be listed in the product information (e.g., summary of product characteristics, labeling, and package leaflet).

Description of accompanying reconstitution diluent(s)

- For FPPs supplied with reconstitution diluent(s) that are commercially available or have been assessed and considered acceptable in connection with another PD with the Authority, a brief description of the reconstitution diluents(s) should be provided.

Type of container and closure

- The container closure used for the FPP (and accompanying reconstitution diluent, if applicable) should be briefly described, with further details provided under 3.1.P.7

3.1.P.2 Pharmaceutical Development (Name, Dosage Form)

- The Pharmaceutical Development section should contain information on the development studies conducted to establish that the dosage form, the formulation, manufacturing process, container closure system, microbiological attributes, and usage instructions are appropriate for the purpose specified in the product dossier.

3.1.P.2.1 Components of the FPP (name, dosage form)

3.1.P.2.1.1 Active pharmaceutical ingredient (name, dosage form)

- The compatibility of the API with excipients listed in 3.1.P.1 should be discussed.

3.1.P.2.1.2 Excipients (name, dosage form)

- When choosing excipients including colouring agents, those with a pharmacopoeia monograph are generally preferred. Other resources are available for information on acceptable excipients and their concentrations, such as the FDA IIG list and the *Handbook of Pharmaceutical Excipients*.

- Use of excipients in concentrations outside of established ranges are discouraged and generally requires justification.
- Where relevant, compatibility study results (e.g., compatibility of a primary or secondary amine API with lactose) should be included to justify the choice of excipients. Specific details should be provided where necessary (e.g., use of potato or corn starch).
- Where preservatives and antioxidants are included in the formulation, the effectiveness of the proposed concentration of the antioxidant as well as its safety should be justified and verified by appropriate studies.

3.1.P.2.2.1 Formulation development (name, dosage form)

- A brief summary describing the development of the FPP should be provided, taking into consideration the proposed route of administration and usage. The differences between the comparative bioavailability or biowaiver formulations and the formulation (i.e., composition) described in 3.1.P.1 should be discussed. Results from comparative in vitro studies (e.g., dissolution) or comparative in vivo studies (e.g., bioequivalence) should be discussed, when appropriate.
- The requirements for bioequivalence studies should be taken into consideration, for example, when formulating multiple strengths and/or when the product(s) may be eligible for a biowaiver. Product clinical information, including bioequivalence and biowaiver justification, should be documented under Module 5.
- If the proposed FPP is a functionally scored tablet, a study should be undertaken to ensure the uniformity of dose in the tablet fragments.

In vitro dissolution or drug release

- A discussion should be included as to how the development of the formulation relates to development of the dissolution method(s) and the generation of the dissolution profile whereas the finished product quality specifications are in-house.
- Recommendations for conducting and assessing comparative dissolution profiles can be found in *WHO Technical* Report *Series*, No. 863 - Thirty-fourth Report and WHO Technical Report Series, No. 937, 2006.

3.1.P.2.2.2 Overages (name, dosage form)

- Any overages in the formulation(s) described in 3.1.P.1 should be justified.
- Justification of an overage to compensate for loss during manufacture should be provided, including the step(s) where the loss occurs, the reasons for the loss, and batch analysis release data (assay results).
- Overages for the sole purpose of extending the shelf-life of the FPP are generally not acceptable.

3.1.P.2.3 Manufacturing process development (name, dosage form)

The selection and optimization of the manufacturing process described in 3.1.P.3.3, in particular its critical aspects, should be explained. Where relevant, justification for the selection of aseptic processing or other sterilization methods over terminal sterilization should be provided.

3.1.P.2.4 Container closure system (name, dosage form)

- The suitability of the container closure system (described in 3.1.P.7) used for the storage, transportation (shipping), and use of the FPP should be discussed. This discussion should consider, e.g., choice of materials, protection from moisture and light, compatibility of the materials of

construction with the dosage form (including sorption to container and leaching) safety of materials of construction, and performance (such as reproducibility of the dose delivery from the device when presented as part of the FPP).

- For a device accompanying a multi-dose container, the results of a study should be provided demonstrating the reproducibility of the device (e.g., consistent delivery of the intended volume), generally at the lowest intended dose.
- A sample of the device should be provided in Module 1.

3.1.P.2.5 Microbiological attributes (name, dosage form)

- Where appropriate, the microbiological attributes of the dosage form should be discussed, including, for example, the rationale for not performing microbial limits testing for non-sterile products and the selection and effectiveness of preservative systems in products containing antimicrobial preservatives. For sterile products, the integrity of the container closure system to prevent microbial contamination should be addressed.
- Where an antimicrobial preservative is included in the formulation, the amount used should be justified by submission of results of the product formulated with different concentrations of the preservative(s) to demonstrate the least necessary but still effective concentration. The effectiveness of the agent should be justified and verified by appropriate studies (e.g., USP or Ph.Eur. general chapters on antimicrobial preservatives) using a batch of the FPP.
- If the lower bound limit for the proposed acceptance criterion for the assay of the preservative is less than 90.0%, the effectiveness of the agent should be established with a batch of the FPP containing a concentration of the antimicrobial preservative corresponding to the lower proposed acceptance criteria.

3.1.P.2.6 Compatibility (name, dosage form)

- The compatibility of the FPP with reconstitution diluent(s) or dosage devices (e.g., precipitation of API in solution, sorption on injection vessels, stability) should be addressed to provide appropriate and supportive information for the labeling.
- Where a device is required for oral liquids or solids (e.g., solutions, emulsions, suspensions and powders/granules for such reconstitution) that are intended to be administered immediately after being added to the device, the compatibility studies mentioned in this Guideline are not required.
- Where sterile, reconstituted products are to be further diluted, compatibility should be demonstrated with all diluents over the range of dilution proposed in the labeling. These studies should preferably be conducted on aged samples. Where the labeling does not specify the type of containers, compatibility (with respect to parameters such as appearance, pH, assay, levels of individual and total degradation products, sub visible particulate matter, and extractables from the packaging components) should be demonstrated in glass, PVC, and polyolefin containers. However, if one or more containers are identified in the labeling, compatibility of admixtures needs to be demonstrated only in the specified containers.
- Studies should cover the duration of storage reported in the labeling (e.g., 24 hours under controlled room temperature and 72 hours under refrigeration).

3.1.P.3 Manufacture (name, dosage form)

3.1.P.3.1 Manufacturer(s) (name, dosage form)

- The name, address, and responsibility of each manufacturer, including contractors, and each proposed production site or facility involved in manufacturing and testing should be provided.
- The facilities involved in the manufacturing, packaging, labeling and testing should be listed. If certain companies are responsible only for specific steps (e.g., manufacturing of an intermediate) such should be clearly indicated in the dossier.
- The list of manufacturers/companies should specify the *actual addresses* of production or manufacturing site(s) involved (including block(s) and unit(s)), rather than the administrative offices.
- For a mixture of an API with an excipient, the blending of the API with the excipient is considered to be the critical step in the manufacture of the final product and therefore the mixture does not fall under the definition of an API. The only exceptions are in the cases where the API cannot exist on its own. Similarly, for a mixture of APIs, the blending of the APIs is considered to be the critical step in the manufacture of the final product. Sites for such manufacturing steps should be included in this section.
- For each site where the major production step(s) are carried out, when applicable, attach a WHO-type certificate of product issued by a competent authority in terms of the WHO Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce (Module 1).
- When there are differences between the product for which this application is submitted and that marketed in the country/countries which provided the WHO-type certificate(s), provide data to support the applicability of the certificate(s) despite the differences. Depending on the case, it may be necessary to provide validation data for differences in site of manufacture, specifications, formulation, etc. Note that only minor differences are likely to be acceptable.

3.1.P.3.2 Batch formula (name, dosage form)

- A batch formula should be provided that includes a list of all components of the dosage form to be used in the manufacturing process, their amounts on a per batch basis, including overages, and a reference to their quality standards.
- The tables in the PD template should be used to summarize the batch formula of the FPP *for each proposed commercial batch size* and express the quantity of each component on a per batch basis, including a statement of the total weight or measure of the batch.
- All components used in the manufacturing process should be included, including those that may not be added to every batch (e.g., acid and alkali), those that may be removed during processing (e.g., solvents) and any others (e.g., nitrogen, silicon for stoppers). If the FPP is formulated using an active moiety, then the composition for the active ingredient should be clearly indicated (e.g., 1 kg of active ingredient base = 1.075 kg active ingredient hydrochloride). All overages should be clearly indicated (e.g., Contains 5 kg (corresponding to 2%) overage of the API to compensate for manufacturing losses).
- The components should be declared by their proper or common names, quality standards (e.g., Ph.Int.,Ph.Eur., BP, USP, JP, House) and, if applicable, their grades (e.g., Microcrystalline Cellulose NF (PH 102)) and special technical characteristics (e.g., lyophilized, micronized, solubilized, emulsified).

3.1.P.3.3 Description of manufacturing process and process controls (name, dosage form)

- A flow diagram should be presented giving the steps of the process and showing where materials enter the process. The critical steps and points at which process controls, intermediate tests or final product controls are conducted should be identified.
- A narrative description of the manufacturing process, including packaging that represents the sequence of steps undertaken and the scale of production should also be provided. Novel processes or technologies and packaging operations that directly affect product quality should be described with a greater level of detail. Equipment should, at least, be identified by type (e.g., tumble blender, in-line homogenizer) and working capacity, where relevant.
- Steps in the process should have the appropriate process parameters identified, such as time, temperature, or pH associated numeric values can be presented as an expected range. Numeric ranges for critical steps should be justified in Section 3.1.P.3.4. In certain cases, environmental conditions (e.g., low humidity for an effervescent product) should be stated.
- The maximum holding time for bulk FPP prior to final packaging should be stated. The holding time should be supported by the submission of stability data, if longer than 30 days. For an aseptically processed sterile product, the holding of the filtered product and sterilized component prior to filling should be under UDLAF (Class A) system and filling should be done immediately within 24hrs.
- Proposals for the reprocessing of materials should be justified. Any data to support this justification should be either referenced to development section or filed in this section
- The information above should be summarized in the DOS-PD template and should reflect the production of the proposed commercial batches. For the manufacture of sterile products, the class (e.g., class A, B, C, etc.) of the areas should be stated for each activity (e.g., compounding, filling, sealing, etc.), as well as the sterilization parameters for equipment, container/closure, terminal sterilization etc.

3.1.P.3.4 Controls of critical steps and intermediates (name, dosage form)

- **Critical Steps:** Tests and acceptance criteria should be provided (with justification, including experimental data) performed at the critical steps identified in 3.1.P.3.3 of the manufacturing process, to ensure that the process is controlled.
- **Intermediates:** Information on the quality and control of intermediates isolatP.3.4ed during the process should be provided.
- Examples of applicable in-process controls include:

a) granulations: moisture (limits expressed as a range), blend uniformity (e.g., low dose tablets), bulk and tapped densities, particle size distribution;

b) solid oral products: average weight, weight variation, hardness, thickness, friability, and disintegration checked periodically throughout compression, weight gain during coating;

c) semi-solids: viscosity, homogeneity, pH;

d) transdermal dosage forms: assay of API-adhesive mixture, weight per area of coated patch without backing;

e) metered dose inhalers: fill weight/volume, leak testing, valve delivery;

f) dry powder inhalers: assay of API-excipient blend, moisture, weight variation of individually contained doses such as capsules or blisters;

g) liquids: pH, specific gravity, clarity of solutions; and,

h) parenterals: appearance, clarity, fill volume/weight, pH, filter integrity tests, particulate matter, leak testing of ampoules.

[Reference: ICH Guidelines Q2, Q6A, Q8, Q9, Q10; WHO Technical Report Series, No. 929, Annex 5]

3.1.P.3.5 Process validation and/or evaluation (name, dosage form)

- Description, documentation, and results of the validation and/or evaluation studies should be provided for critical steps or critical assays used in the manufacturing process (e.g., validation of the sterilization process or aseptic processing or filling). Viral safety evaluation should be provided in 3.1A.2, if necessary.
- For products that meet the criteria of an *established multisource product*, a product quality review as outlined in Appendix 1 may be submitted in lieu of the information below.
- The following information should be provided for all other products:
- a copy of the *process validation protocol*, specific to this FPP, that identifies the critical equipment and process parameters that can affect the quality of the FPP and defines testing parameters, sampling plans, analytical procedures and acceptance criteria;
- a *commitment* that three consecutive, production-scale batches of this FPP will be subjected to *prospective validation* in accordance with the above protocol. The applicant should submit a written commitment that information from these studies will be available for verification after registration by the Authority inspection team; and,
- if the process validation studies have already been conducted (e.g., for sterile products), a copy of the *process validation report* should be provided in the PD in lieu of (a) and (b) above.

- One of the most practical forms of process validation, mainly for non-sterile products, is the final testing of the product to an extent greater than that required in routine quality control. It may involve extensive sampling, far beyond that called for in routine quality control and testing to normal quality control specifications and often for certain parameters only. Thus, for instance, several hundred tablets per batch may be weighed to determine unit dose uniformity. The results are then treated statistically to verify the "normality" of the distribution and to determine the standard deviation from the average weight. Confidence limits for individual results and for batch homogeneity are also estimated. Strong assurance is provided that samples taken at random will meet regulatory requirements if the confidence limits are well within pharmacopoeia specifications.
- Similarly, extensive sampling and testing may be performed with regard to any quality requirements. In addition, intermediate stages may be validated in the same way, e.g., dozens of samples may be assayed individually to validate mixing or granulation stages of low-dose tablet production by using the content uniformity test. Products (intermediate or final) may occasionally be tested for non-routine characteristics. Thus, sub visual particulate matter in parenteral preparations may be determined by means of electronic devices, or tablets/capsules tested for dissolution profile, if such tests are not performed on every batch.

- Where ranges of batch sizes are proposed, it should be shown that variations in batch size would not adversely alter the characteristics of the finished product. It is envisaged that those parameters listed in the following validation scheme will need to be re-validated once further scale-up is proposed after registration.
- The process validation protocol should include inter alia the following:
- a reference to the current master production document;
- a discussion of the critical equipment;

- the process parameters that can affect the quality of the FPP (critical process parameters (CPPs)), including challenge experiments and failure mode operation;
- details of the sampling—sampling points, stages of sampling, methods of sampling, and the sampling plans (including schematics of blender/storage bins for uniformity testing of the final blend);
- the testing parameters/acceptance criteria including in-process and release specifications and including comparative dissolution profiles of validation batches against the batch(es) used in the bioavailability or biowaiver studies;
- the analytical procedures or a reference to appropriate section(s) of the dossier;
- the methods for recording/evaluating results; and,
- the proposed timeframe for completion of the protocol.

- The manufacture of sterile FPPs needs a well-controlled manufacturing area (e.g., a strictly controlled environment, highly reliable procedures, and appropriate in-process controls). A detailed description of these conditions, procedures and controls should be provided, together with actual copies of the following standard operating procedures:
- washing, treatment, sterilizing, and depyrogenating of containers, closures, and equipment;
- filtration of solutions;
- lyophilization process;
- leaker test of filled and sealed ampoules;
- final inspection of the product;
- sterilization cycle; and,
- routine environmental monitoring and media fill validation exercise.

- The sterilization process used to destroy or remove microorganisms is probably the single most important process in the manufacture of parenteral FPPs. The process can make use of moist heat (e.g., steam), dry heat, filtration, gaseous sterilization (e.g., ethylene oxide), or radiation. It should be noted that terminal steam sterilization, when practical, is considered to be the method of choice to ensure sterility of the final FPP. Therefore, scientific justification for selecting any other method of sterilization should be provided.
- The sterilization process should be described in detail and evidence should be provided to confirm that it will produce a sterile product with a high degree of reliability and that the physical and chemical properties as well as the safety of the FPP will not be affected. Details, such as Fo range, temperature range, and peak dwell time for an FPP and the container closure should be provided. Although standard autoclaving cycles of 121°C for 15 minutes or more would not need a detailed rationale; such justifications should be provided for reduced temperature cycles or elevated temperature cycles with shortened exposure times. If ethylene oxide is used, studies and acceptance criteria should control the levels of residual ethylene oxide and related compounds.
- Filters used should be validated with respect to pore size, compatibility with the product, absence of extractable, and adsorption of the API or any of the components.
- For the validation of aseptic filling of parenteral products that cannot be terminally sterilized, simulation process trials should be conducted. This involves filling ampoules with culture media under normal conditions, followed by incubation and control of microbial growth. A level of contamination of less than 0.1% is considered to be acceptable.[Reference: ICH Guidelines Q8, Q9, Q10; WHO Technical Report Series, Nos. 902 and 908]

3.1.P.4 Control of Excipients (Name, Dosage Form)

3.1.P.4.1 Specifications (name, dosage form)

- The specifications from the applicant or the FPP manufacturer should be provided for all excipients, including those that may not be added to every batch (e.g., acid and alkali), those that do not appear in the final FPP (e.g., solvents) and any others used in the manufacturing process (e.g., nitrogen, silicon for stoppers).
- If the standard claimed for an excipient is an officially recognized pharmacopoeia standard, it is sufficient to state that the excipient is tested according to the requirements of that standard, rather than reproducing the specifications found in the officially recognized pharmacopoeia monograph.
- If the standard claimed for an excipient is a non-pharmacopoeia standard (e.g., House standard) or includes tests that are supplementary to those appearing in the officially recognized pharmacopoeia monograph, a copy of the specification for the excipient should be provided.
- For excipients of natural origin, microbial limit testing should be included in the specifications. Skip testing is acceptable, if justified (submission of acceptable results of five production batches).
- For oils of plant origin (e.g., soy bean oil, peanut oil), the absence of aflatoxins or biocides should be demonstrated.
- The colors permitted for use are limited to those listed in the ―Japanese pharmaceutical excipients, the EU ―List of permitted food colors, and the US FDA ―Inactive ingredient guide. For proprietary mixtures, the supplier's product sheet with the qualitative formulation should be submitted, in addition to the FPP manufacturer's specifications for the product, including identification testing.
- For flavors, the qualitative composition should be submitted, as well as a declaration that the excipients comply with foodstuff regulations (e.g., US FDA or EU).
- Information that is considered confidential may be submitted directly to the Authority by the supplier with reference to the specific related product.
- Other certifications of at-risk components may be required on a case-by-case basis.
- If additional purification is undertaken on commercially available excipients, details of the process of purification and modified specifications should be submitted.

3.1.P.4.2 Analytical procedures (name, dosage form)

- The analytical procedures used for testing the excipients should be provided, where appropriate.
- Copies of analytical procedures from officially recognized pharmacopoeia monographs do not need to be submitted.

3.1.P.4.3 Validation of analytical procedures (name, dosage form)

- Copies of analytical validation information are generally not submitted for the testing of excipients, with the exception of the validation of in-house methods where appropriate.

3.1.P.4.4 Justification of specifications (name, dosage form)

- A discussion of the tests that are supplementary to those appearing in the officially recognized pharmacopoeia monograph should be provided.

3.1.P.4.5 Excipients of human or animal origin (name, dosage form)

- For excipients of human or animal origin, information should be provided regarding adventitious agents (e.g., sources, specifications, description of the testing performed, viral safety data). For more detail, see Section 3.1.A.2.
- The following excipients should be addressed in this section: gelatin, phosphates, stearic acid, magnesium stearate and other stearates. If from plant origin a declaration to this effect will suffice.
- For these excipients from animal origin, a letter of attestation should be provided confirming that the excipients used to manufacture the FPP are *without* risk of transmitting agents of animal spongiform encephalopathies.
- Materials of animal origin should be avoided whenever possible.

3.1.P.4.6 Novel excipients (name, dosage form)

- For excipient(s) used for the first time in an FPP or by a new route of administration, full details of manufacture, characterization , and controls, with cross references to supporting safety data (nonclinical and/or clinical) should be provided according to the API and/or FPP intended purpose. (Details should be provided in 3.1.A.3).

3.1.P.5 Control of FPP (name, dosage form)

3.1.P.5.1 Specification(s) (name, dosage form)

- A copy of the FPP specification(s) from the applicant (as well as the company responsible for the batch release of the FPP, if different from the applicant), dated and signed by authorized personnel (i.e., the person in charge of the quality control or quality assurance department) should be provided in the PD.
- The specifications should be summarized according to the tables in the PD template including the tests, acceptance criteria and analytical procedures (including types, sources and versions for the methods):
- the *standard* declared by the applicant could be an officially recognized pharmacopoeia standard (e.g., Ph.Int., BP, USP, JP) or a House (manufacturer's) standard;
- the *specification reference number and version (e.g., revision number and/or date)* should be provided for version control purposes; and,
- for the analytical procedures, the *type* should indicate the kind of analytical procedure used (e.g., visual, IR, UV, HPLC), the *source* refers to the origin of the analytical procedure (e.g., Ph.Int., Ph.Eur., BP, USP, JP, in-house), and the *version (e.g., code number/version/date)* should be provided for version control purposes.
- Specifications should include, at minimum, tests for appearance, identification, assay, purity, pharmaceutical tests (e.g., dissolution), physical tests (e.g., loss on drying, hardness, friability, particle size, apparent density), uniformity of dosage units, identification of coloring materials, identification and assay of antimicrobial or chemical preservatives (e.g., antioxidants), and microbial limit tests.
- The following information provides guidance for specific tests:

a) fixed-dose combination FPPs (FDC-FPPs):

- analytical methods that can distinguish each API in the presence of the other API(s) should be developed and validated,
- acceptance criteria for degradation products should be established with reference to the API they are derived from. If an impurity results from a chemical reaction between two or more APIs, its acceptance limits should be calculated with reference to the worst case (the API with the smaller area under the curve). Alternatively the content of such impurities could be calculated in relation to their reference standards,
- when any one API is present at less than 25 mg or less than 25% of the weight of the dosage unit, a test and limit for content uniformity is required for each API in the FPP,
- when all APIs are present at equal or greater than 25 mg and equal or greater than 25% of the weight of the dosage unit, a test and limit for weight variation may be established for the FPP, in lieu of content uniformity testing;

- modified-release products: a meaningful API release method;

b) inhalation and nasal products:

- consistency of delivered dose (throughout the use of the product), particle or droplet size distribution profiles (comparable to the product used in in-vivo studies, where applicable) and if applicable for the dosage form, moisture content, leak rate, microbial limits, preservative assay, sterility and weight loss;

c) suppositories: uniformity of dosage units, melting point;

d) transdermal dosage forms: peal or shear force, mean weight per unit area, dissolution; and,

e) sterile: sterility, endotoxin.

- Unless there is appropriate justification, the acceptable limit for the API content of the FPP in the release specifications is ± 5% of the label claim (i.e., 95.0-105.0%).
- Skip testing is acceptable for parameters such as identification of coloring materials and microbial limits, when justified by the submission of acceptable supportive results for five production batches. When skip testing justification has been accepted, the specifications should include a footnote, stating at minimum the following skip testing requirements: at minimum, every tenth batch and at least one batch annually is tested. In addition, for stability-indicating parameters such as microbial limits, testing will be performed at release and shelf-life during stability studies.
- Any differences between release and shelf-life tests and acceptance criteria should be clearly indicated and justified. Note that such differences for parameters, such as dissolution and moisture content, are normally not accepted.[Reference: ICH Guidelines Q3B, Q3C, Q6A; official monograph]

3.1.P.5.2 Analytical procedures (name, dosage form)

- Copies of the in-house analytical procedures used during pharmaceutical development (if used to generate testing results provided in the PD) as well as those proposed for routine testing should be provided. Unless modified, it is not necessary to provide copies of officially recognized pharmacopoeia analytical procedures.
- Tables for summarizing a number of the different analytical procedures and validation information (e.g., HPLC assay/impurity methods) can be found in the 2.3.R Regional information section of the QOS-PD (i.e., *2.3.R.2)*. These tables should be used to summarize the analytical procedures used for determination of the assay, related substances and dissolution of the FPP.
- Refer to Section 3.1.S.4.2 of this Guideline for additional guidance on analytical procedures.

3.1.P.5.3 Validation of analytical procedures (name, dosage form)

- Copies of the validation reports for the in-house analytical procedures used during pharmaceutical development (if used to support testing results provided in the PD) as well as those proposed for routine testing should be provided.
- Tables for summarizing a number of the different analytical procedures and validation information (e.g., HPLC assay/impurity methods, GC methods) can be found in the 2.3.R Regional information section of the QOS-PD (i.e., *2.3.R.2).*These tables should be used to summarize the validation information of the analytical procedures used for determination of the assay, related substances, and dissolution of the FPP.
- As recognized by regulatory authorities and pharmacopoeias themselves, verification of pharmacopoeia methods can be necessary. The pharmacopoeia methods, as published, are typically validated based on an API or an FPP originating from a specific manufacturer. Different sources of the same API or FPP can contain impurities and/or degradation products or excipients that were not considered during the development of the monograph. Therefore, the monograph and pharmacopoeia method(s) should be demonstrated suitable for the control of the proposed FPP.
- For officially recognized pharmacopoeia FPP *assay* methods, verification should include a demonstration of specificity, accuracy, and repeatability (method precision).If an officially recognized pharmacopoeia method is used to control related substances that are not specified in the monograph, full validation of the method is expected with respect to those related substances.
- If an officially recognized pharmacopoeia standard is claimed and an in-house method is used in lieu of the pharmacopoeia method (e.g., for assay or for related compounds), equivalency of the in-house and pharmacopoeia methods should be demonstrated. This could be accomplished by performing duplicate analyses of one sample by both methods and providing the results from the study. For related compound methods, the sample analyzed should be the placebo spiked with related compounds at concentrations equivalent to their specification limits.

3.1.P.5.4 Batch analyses (name, dosage form)

- Information should include strength and batch number, batch size, date and site of production and use (e.g., used in comparative bioavailability or biowaiver studies, preclinical and clinical studies (if relevant), stability, pilot, scale-up and, if available, production-scale batches) on relevant FPP batches used to establish the specification(s) and evaluate consistency in manufacturing.
- Analytical results tested by the company responsible for the batch release of the FPP (generally, the applicant or the FPP manufacturer, if different from the applicant) should be provided for not less than two batches of commercial scale
- The discussion of results should focus on observations noted for the various tests, rather than reporting comments such as ―all tests meet specifications. This should include ranges of analytical results, where relevant. For quantitative tests (e.g., individual and total impurity tests and assay tests), it should be ensured that actual *numerical results* are provided rather than vague statements such as ―within limits or ―conforms (e.g., ―levels of degradation product A ranged from 0.2 to 0.4 %). Dissolution results should be expressed at minimum as both the average and range of individual results.
- A discussion and justification should be provided for any incomplete analyses (e.g., results not tested according to the proposed specification).[Reference: ICH Guidelines Q3B, Q3C, Q6A; official monograph]

3.1.P.5.5 Characterization of impurities (name, dosage form)

- A discussion should be provided of all impurities that are potential degradation products (including those among the impurities identified in 3.1.S.3.2 as well as potential degradation products resulting from interaction of the API with other APIs (FDCs), excipients, or the container closure system) and FPP process-related impurities (e.g., residual solvents in the manufacturing process for the FPP). [Reference: ICH Guidelines Q3B, Q3C, Q6A]

3.1.P.5.6 Justification of specification(s) (name, dosage form)

- A discussion should be provided on the omission or inclusion of certain tests, evolution of tests, analytical procedures and acceptance criteria, differences from the officially recognized pharmacopoeia standard(s), etc. If the officially recognized pharmacopoeia methods have been modified or replaced, a discussion should be included.
- The justification for certain tests, analytical procedures, and acceptance criteria (e.g., degradation products, dissolution method development) may have been discussed in other sections of the PD and does not need to be repeated here, although a cross-reference to its location should be provided.
- ICH Guideline Q6A should be consulted for the development of specifications for FPPs.

3.1.P.6 Reference standards or materials (name, dosage form)

- Information on the reference standards or reference materials used for testing of the FPP should be provided, if not previously provided in ―3.1.S.5 Reference Standards or Materials.
- See Section 3.1.S.5 for information that should be provided on reference standards or materials. Information should be provided on reference materials of FPP degradation products, where not included in 3.1.S.5.[Reference: ICH Guideline Q6A; WHO Technical Report Series, No. 943, Annex 3]

3.1.P.7 Container Closure System (name, dosage form)

- A description of the container closure systems should be provided, including the identity of materials of construction of each primary packaging component and its specification. The specifications should include description and identification (and critical dimensions, with drawings where appropriate). Non-pharmacopoeia methods (with validation) should be included, where appropriate.
- For non-functional secondary packaging components (e.g., those that neither provide additional protection nor serve to deliver the product), only a brief description should be provided. For functional secondary packaging components, additional information should be provided.
- Suitability information should be located in 3.1.P.2.
- The WHO *Guidelines on packaging for pharmaceutical products* (WHO Technical Report Series, No. 902, Annex 9, 2002) and the officially recognized pharmacopoeias should be consulted for recommendations on the packaging information for FPPs.
- Descriptions, materials of construction and specifications (of the company responsible for packaging the FPP, generally the FPP manufacturer) should be provided for the packaging components that are:
  - in direct contact with the dosage form (e.g., container, closure, liner, desiccant, filler);

- used for drug delivery (including the device(s) for multi-dose solutions, emulsions, suspensions, and powders/granules for such);
- used as a protective barrier to help ensure stability or sterility; and,
- necessary to ensure FPP quality during storage and shipping.

- The specifications for the primary packaging components should include a specific test for identification (e.g., IR).Specifications for film and foil materials should include limits for thickness or area weight.
- Information to establish the suitability (e.g., qualification) of the container closure system should be discussed in Section 3.1.P.2.

3.1.P.8 Stability (Name, Dosage Form)

3.1.P.8.1 Stability summary and conclusions (name, dosage form)

- The types of studies conducted, protocols used, and the results of the studies should be summarized. The summary should include, for example, conclusions with respect to storage conditions and shelf-life, and, if applicable, in-use storage conditions and shelf-life.

Stress testing

- Photostability testing should be conducted on at least one primary batch of the FPP, if appropriate. If "protect from light" is stated in one of the officially recognized pharmacopoeias for the API or FPP, it is sufficient to state "protect from light" on labeling, in lieu of photostability studies, when the container closure system is shown to be light protective. Additional stress testing of specific types of dosage forms may be appropriate (e.g., cyclic studies for semi-solid products, freeze-thaw studies for liquid products).

Accelerated, intermediate (if necessary) and long-term testing

- Stability data must demonstrate stability of the medicinal product throughout its intended shelf-life under the climatic conditions of Sri Lanka. Refer to WHO Technical Report Series, No. 953, Annex 2, Appendix 1, for information on climatic zones. According to Annex 2,Appendix 1, the required long-term storage conditions for Sri Lanka is 30ºC±2ºC/75%±5%RH. The minimum long-term storage condition should thus fulfill the storage conditions 30ºC±2ºC/75%±5%RH, as recommended by WHO, can also be acceptable. The use of alternative long-term conditions will need to be justified and should be supported with appropriate evidence.
- Other storage conditions are outlined in the WHO stability guideline for FPPs packaged in impermeable and semi-permeable containers and those intended for storage in a refrigerator and in a freezer. FPPs intended for storage below -20°C should be treated on a case-by-case basis.
- The minimum data required at the time of submission of the dossier (in general):

Storage temperature (ºC)	**Relative humidity (%)**	**Minimum time period (months)**
Accelerated 40±2	75±5	6
Long-term 30±2	65±5 or 75±5	To cover the complete shelf-life

The information on the stability studies should include details such as

a) storage conditions;
b) strength;

c) batch number, including the API batch number(s) and manufacturer(s);
d) batch size;
e) container closure system, including orientation (e.g., erect, inverted, on-side), where applicable; and,
f) completed test intervals.

- The discussion of test results should focus on observations noted for the various tests, rather than reporting comments such as ―all tests meet specifications.‖ This should include ranges of analytical results and any trends that were observed. For quantitative tests (e.g., individual and total degradation product tests and assay tests), it should be ensured that actual numerical results are provided rather than vague statements such as ―within limits or ―conforms. Dissolution results should be expressed at minimum as both the average and range of individual results.
- Applicants should consult the ICH Q1E guidance document for details on the evaluation and extrapolation of results from stability data (e.g., if significant change was not observed within six months at accelerated condition and the data show little or no variability, the proposed shelf-life could be up to two times the period covered by the long-term data, but should not exceed the long-term data by 12 months).

Proposed storage statement and shelf-life

- The proposed storage statement and shelf-life (and in-use storage conditions and in-use period, if applicable) for the FPP should be provided.[Reference: WHO TRS No. 953, Annex 2; ICH Guidelines Q1A, Q1B, Q1C, Q1D, Q1E, Q3B, Q6A]

3.1.P.8.2 Post-approval stability protocol and stability commitment (name, dosage form)
Primary stability study commitment

- When available long-term stability data on primary batches do not cover the proposed shelf-life granted at the time of assessment of the PD, a commitment should be made to continue the stability studies in order to firmly establish the shelf-life.
- A written commitment (signed and dated) to continue long-term testing over the shelf-life period should be included in the dossier.

Commitment stability studies

- The long-term stability studies for the *commitment batches* should be conducted through the proposed shelf-life on at least three production batches of each strength in each container closure system. Where stability data was not provided for three production batches of each strength, a written commitment (signed and dated) should be included in the dossier.

Ongoing stability studies

- An *ongoing stability program* is established to monitor the product over its shelf-life and to determine that the product remains and can be expected to remain within specifications under the storage conditions on the label. Unless otherwise justified, at least one batch per year of product manufactured in every strength and in every container closure system, if relevant, should be included in the stability program (unless none is produced during that year).
- Bracketing and matrixing may be applicable. A written commitment (signed and dated) to this effect should be included in the dossier.
- Any differences in the stability protocols used for the primary batches and those proposed for the *commitment batches* or *ongoing batches* should be scientifically justified.

3.1.P.8.3 Stability data (name, dosage form)

- Results of the stability studies should be presented in an appropriate format (e.g., tabular, graphical, narrative). Information on the analytical procedures used to generate the data and validation of these procedures should be indicated.
- The actual stability results/reports used to support the proposed shelf-life should be provided in the PD. For quantitative tests (e.g., individual and total degradation product tests and assay tests), it should be ensured that actual numerical results are provided rather than vague statements such as ―within limits‖ or ―conforms.‖ Dissolution results should be expressed, at minimum, as both the average and range of individual results.

3.1.A Appendices

3.1.A.1 Facilities and Equipment

Not applicable except for biotech products.

3.1.A.2 Adventitious Agents Safety Evaluation

Provide details of any viral safety evaluation of blood biotech products.

3.1.A.3 Novel Excipients

Provide details of safety (refer to Module 4) and clinical documentation (refer to Module 5) for excipients used for the first time and not used in similar SRA-approved products.

3.1.R Regional Information

3.1.R.1 Production Documentation

3.1.R.1.1 Executed production documents

A minimum of three batches of commercial scale, should have been manufactured for each strength at the time of submission.

This condition could be exempted by the NMRA if the medicine is a medicine for orphan diseases, a drug considered as "orphan" to Sri Lanka by the NMRA and a drug for emergency situations. The executed production documents of two pilot scale batches should be submitted in this situation and these batches should be manufactured by a procedure fully representative of and simulating that to be applied to a full production-scale batch.

English translations of executed records should be provided, where relevant

MODULE 4:

NON-CLINICAL STUDY REPORTS

This section of the Guideline is not required for generic products in which a molecule (s) of FPP is registered in NMRA of . In such cases, reference to the list suffices.

4.1 Table of Contents of Module 4

A Table of Contents should be provided that lists all of the nonclinical study reports and gives the location of each study report in the PD.

4.2 Study Reports

The study reports should be presented in the following order:

4.2.1 Pharmacology

4.2.1.1 Primary Pharmacodynamics

4.2.1.2 Secondary Pharmacodynamics

4.2.1.3 Safety Pharmacology

4.2.1.4 Pharmacodynamic Drug Interactions

4.2.2 Pharmacokinetics

4.2.2.1 Analytical Methods and Validation Reports (if separate reports are available)

4.2.2.2 Absorption

4.2.2.3 Distribution

4.2.2.4 Metabolism

4 2.2.5 Excretion

4.2.2.6 Pharmacokinetic Drug Interactions (nonclinical)

4.2.2.7 Other Pharmacokinetic Studies

4.2.3 Toxicology

4.2.3.1 Single-Dose Toxicity (in order by species, by route)

4.2.3.2 Repeat-Dose Toxicity (in order by species, by route, by duration)

4.2.3.3 Genotoxicity

4.2.3.3.1 In vitro

4.2.3.3.2 In vivo (including supportive toxicokinetics evaluations)

4.2.3.4 Carcinogenicity (including supportive toxicokinetics evaluations)

4.2.3.4.1 Long-term studies (in order by species, including range-finding studies that cannot appropriately be included under repeat-dose toxicity or pharmacokinetics)

4.2.3.4.2 Short- or medium-term studies (including range-finding studies that cannot appropriately be included under repeat-dose toxicity or pharmacokinetics)

4.2.3.4.3 Other studies

4.2.3.5 Reproductive and Developmental Toxicity (including range-finding studies and supportive toxicokinetics evaluations) [If modified study designs are used, the following sub-headings should be modified accordingly.]

4.2.3.5.1 Fertility and early embryonic development

4.2.3.5.2 Embryo-fetal development

4.2.3.5.3 Prenatal and postnatal development, including maternal function
4.2.3.5.4 Studies in which the offspring (juvenile animals) are dosed and/or further evaluated
4.2.3.6 Local Tolerance
4.2.3.7 Other Toxicity Studies (if available)
4.2.3.7.1 Antigenicity
4.2.3.7.2 Immunotoxicity
4.2.3.7.3 Mechanistic studies (if not included elsewhere)
4.2.3.7.4 Dependence
4.2.3.7.5 Metabolites
4.2.3.7.6 Impurities
4.2.3.7.7 Other

4.3 Literature References

MODULE 5:

CLINICAL STUDY REPORTS

This section of the Guideline is applicable only for medicines where a BE study is a requirement and where the medicine is not yet registered in . For FPPs in which the molecule(s) is new to the n market, the applicant should submit full safety and efficacy data as outline in this Guideline.

For multisource generic products having a molecule(s) already registered in and requiring BE study, only section 5.3.3 of Module 5 needs to be supported with actual experimental evidence and where applicable reference to literature can be considered for other section.

For generic products requiring clinical equivalence study, in cases where comparative clinical evidence of a pharmacokinetics (PK) BE study cannot be conducted, section 5.3.4 of Module 5 may be required, to be determined on a case-by-case basis.

The information provided below is not intended to indicate what studies are required for successful registration. It indicates an appropriate organization for the clinical study reports that need to be submitted with the application.

The placement of a report should be determined by the primary objective of the study. Each study report should appear in only one section. Where there are multiple objectives, the study should be cross-referenced in the various sections. An explanation, such as "not applicable" or "no study conducted", should be provided when no report or information is available for a section or subsection.

5.1 Table of Contents of Module 5

5.2 Tabular Listing of All Clinical Studies

A tabular listing of all clinical studies and related information should be provided. For each study, this tabular listing should generally include the type of information identified in Table 5.1 of this Guideline. Other information can be included in this table if the applicant considers it useful. The sequence in which the studies are listed should follow the sequence described in Section 5.3 below. Use of a different sequence should be noted and explained in an introduction to the tabular listing.

5.3 Clinical Study Reports

5.3.1 Reports of Biopharmaceutical Studies

BA studies evaluate the rate and extent of release of the active substance from the medicinal product. Comparative BA or BE studies may use PK, PD, clinical, or in vitro dissolution endpoints, and may be either single dose or multiple dose. When the primary purpose of a study is to assess the PK of a drug, but also includes BA information, the study report should be submitted in Section 5.3.1, and referenced in Sections 5.3.1.1 and/or 5.3.1.2.

5.3.1.1 Bioavailability (BA) study reports

BA studies in this section should include:

studies comparing the release and systemic availability of a drug substance from a solid oral dosage form to the systemic availability of the drug substance given intravenously or as an oral liquid dosage form;

- dosage form proportionality studies; and,
- food-effect studies.

reference to literature suffices for generic products.

5.3.1.2 Comparative BA and BE study reports

Studies in this section compare the rate and extent of release of the drug substance from similar drug products (e.g., tablet to tablet, tablet to capsule). Comparative BA or BE studies may include comparisons between

- the drug product used in clinical studies supporting effectiveness and the to-be-marketed drug product, the drug product used in clinical studies supporting effectiveness, and the drug product used in stability batches; and,
- similar drug products from different manufacturers.

For in vivo bioequivalence studies and waver of bioequivalence requirements, WHO guidelines on registration requirements to establish interchangeability at multisource (generic) pharmaceutical products and other relevant WHO guidelines applies.

5.3.1.3 In vitro–in vivo correlation study reports

In vitro dissolution studies that provide BA information, including studies used in seeking to correlate in vitro data with in vivo correlations, should be placed in section 5.3.1.3. reports of in vitro dissolution tests used for batch quality control and/or batch release should be placed in the Quality section (module 3) of the pd.

5.3.1.4 Reports of bioanalytical and analytical methods for human studies

Bioanalytical and/or analytical methods for biopharmaceutic studies or in vitro dissolution studies should ordinarily be provided in individual study reports. Where a method is used in multiple studies, the method and its validation should be included once in section 5.3.1.4 and referenced in the appropriate individual study reports.

5.3.2 Reports of Studies Pertinent to Pharmacokinetics Using Human Biomaterials

Human biomaterials is a term used to refer to proteins, cells, tissues ,and related materials derived from human sources that are used in vitro or ex vivo to assess PK properties of drug substances. Examples include cultured human colonic cells that are used to assess permeability through biological membranes and transport processes, and human albumin that is used to assess plasma protein binding. Of particular importance is the use of human biomaterials such as hepatocytes and/or hepatic microsomes to study metabolic pathways and to assess drug-drug interactions with these pathways. Studies using biomaterials to address other properties (e.g., sterility or pharmacodynamics) should not be placed in the Clinical Study Reports Section, but in the Nonclinical Study Section (Module 4).

5.3.2.1 Plasma protein binding study reports

Ex vivo protein binding study reports should be provided here. Protein binding data from PK blood and/or plasma studies should be provided in section 5.3.3.

5.3.2.2 Reports of hepatic metabolism and drug interaction studies

Reports of hepatic metabolism and metabolic drug interaction studies with hepatic tissue should be placed here.

5.3.2.3 Reports of studies using other human biomaterials

Reports of studies with other biomaterials should be placed in this section.

5.3.3 Reports of Human Pharmacokinetic (PK) Studies

Assessment of the PK of a drug in healthy subjects and/or patients is considered critical to designing dosing strategies and titration steps, to anticipating the effects of concomitant drug use, and to interpreting observed pharmacodynamic differences.

These assessments should provide a description of the body's handling of a drug over time, focusing on maximum plasma concentrations (peak exposure), area-under-curve (total exposure), clearance, and accumulation of the parent drug and its metabolite(s), in particular, those that have pharmacological activity. The PK studies whose reports should be included in sections 5.3.3.1 and 5.3.3.2 are generally designed to: (1) measure plasma drug and metabolite concentrations over time; (2) measure drug and metabolite concentrations in urine or feces, when useful or necessary; and/or, (3) measure drug and metabolite binding to protein or red blood cells. On occasion, PK studies may include measurement of drug distribution into other body tissues, body organs, or fluids (e.g., synovial fluid or cerebrospinal fluid), and the results of these tissue distribution studies should be included in section 5.3.3.1 to 5.3.3.2, as appropriate.

These studies should characterize the drug's PK and provide information about the absorption, distribution, metabolism, and excretion of a drug and any active metabolites in healthy subjects and/or patients. Studies of mass balance and changes in PK related to dose (e.g., determination of dose proportionality) or time (e.g., due to enzyme induction or formation of antibodies) are of particular interest and should be included in sections 5.3.3.1 and/or 5.3.3.2.

Apart from describing mean PK in normal and patient volunteers, PK studies should also describe the range of individual variability. The study of human PK study reports should fulfill the requirements for bioequivalence as described in Annex IV of this Guideline.

5.3.3.1 Healthy subject PK and initial tolerability study reports

Reports of PK and initial tolerability studies in healthy subjects should be placed in this section.

5.3.3.2 Patient PK and initial tolerability study reports

Reports of PK and initial tolerability studies in patients should be placed in this section. Most of the time for generic products, cross-reference to literature suffices. However, when PK studies are not possible on healthy subjects because of toxicity and other issues, this section should be completed where applicable.

5.3.3.3 Intrinsic factor PK study reports

Reports of PK studies to assess effects of intrinsic factors, should be placed in this section. Reports of PK studies to assess differences in systemic exposure as a result of changes in PK due to intrinsic (e.g., age, gender, racial, weight, height, disease, genetic polymorphism, and organ dysfunction) factors should be placed in this section.

5.3.3.4 Extrinsic factor PK study reports

Reports of PK studies to assess effects of extrinsic factors (e.g., drug-drug interactions, diet, smoking, and alcohol use) factors should be organized in this section.

5.3.3.5 Population PK study reports

Reports of population PK studies based on sparse samples obtained in clinical trials, including efficacy and safety trials, should be placed in this section.

5.3.4 Reports of Human Pharmacodynamic (PhD) Studies

This section of the Guideline does not require experimental evidence for generic products and medicines already registered in Sri Lanka. Exceptions are when meaningful PK studies cannot be conducted as a result of difficulties, such as inadequate measurement of the active pharmaceutical substance in biological fluids. See Annex IV for further clarification.

Reports of studies with a primary objective of determining the PhD effects of a drug product in humans should be placed in this section. Reports of studies whose primary objective is to establish efficacy or to accumulate safety data, however, should be placed in section 5.3.5.

This section should include reports of: (1) studies of pharmacologic properties known or thought to be related to the desired clinical effects (biomarkers); (2) short-term studies of the main clinical effect; and, (3) PD studies of other properties not related to the desired clinical effect. Because a quantitative relationship of these pharmacological effects to dose and/or plasma drug and metabolite concentrations is usually of interest, PD information is frequently collected in dose response studies or together with drug concentration information in PK studies (concentration-response or PK/PD studies).

Relationships between PK and PD effects that are not obtained in well-controlled studies are often evaluated using an appropriate model and used as a basis for designing further dose-response studies or, in some cases, for interpreting effects of concentration differences in population subsets.

Dose-finding, PD, and/or PK-PD studies can be conducted in healthy subjects and/or patients, and can also be incorporated into the studies that evaluate safety and efficacy in a clinical indication. Reports of dose-finding, PD, and/or PK/PD studies conducted in healthy subjects should be placed in section 5.3.4.1, and the reports for those studies conducted in patients should be placed in section 5.3.4.2.

In some cases, the short-term PD, dose-finding, and/or PK-PD information found in pharmacodynamic studies conducted in patients will provide data that contribute to assessment of efficacy, either because they show an effect on an acceptable surrogate marker (e.g., blood pressure) or on a clinical benefit endpoint (e.g., pain relief). Similarly, a PD study may contain important clinical safety information. When these studies are part of the efficacy or safety demonstration, they are considered clinical efficacy and safety studies that should be included in section 5.3.5, not in section 5.3.4.

5.3.4.1 Healthy subject PD and PK/PD study reports

PD and/or PK/PD studies having non-therapeutic objectives in healthy subjects should be placed in this section.

5.3.4.2 Patient PD and PK/PD study reports

PD and/or PK/PD studies in patients should be submitted in this section.

5.3.5 Reports of Efficacy and Safety Studies

For generic medicines in which the molecule(s) of FPP are registered in Sri Lanka cross reference to literature will suffice. This section should include reports of all clinical studies of efficacy and/or safety carried out with the drug, conducted by the sponsor, or otherwise available, including all completed and all ongoing studies of the drug in proposed and non-proposed indications. The study reports should provide the level of detail appropriate to the study and its role in the application.

In cases where the application includes multiple therapeutic indications, the reports should be organized in a separate section 5.3.5 for each indication. In such cases, if a clinical efficacy study is relevant to only one of the indications included in the application, it should be included in the appropriate section 5.3.5; if a clinical efficacy study is relevant to multiple indications, the study report should be included in the most appropriate section 5.3.5 and referenced as necessary in other sections 5.3.5, for example, section 5.3.5A, section 5.3.5B.

5.3.5.1 Study reports of controlled clinical studies pertinent to the claimed indication

The controlled clinical study reports should be sequenced by type of control:

- Placebo control (could include other control groups, such as an active comparator or other doses);
- No-treatment control;
- Dose-response (without placebo);
- Active control (without placebo); or,
- External (historical) control, regardless of the control treatment.

Within each control type, where relevant to the assessment of drug effect, studies should be organized by treatment duration. Studies of indications other than the one proposed in the application, but that provide support for efficacy in the proposed use, should be included in section 5.3.5.1.

Where a pharmacodynamic study contributes to evidence of efficacy, it should be included in section 5.3.5.1. The sequence in which studies were conducted is not considered pertinent to their presentation. Thus, placebo-controlled trials, whether early or late, should be placed in section 5.3.5.1. Controlled safety studies, including studies in conditions that are not the subject of the application, should also be reported in section 5.3.5.1.

5.3.5.2 Study reports of uncontrolled clinical studies

Study reports of uncontrolled clinical studies (e.g., reports of open label safety studies) should be included in section 5.3.5.2. This includes studies in conditions that are not the subject of the marketing application.

5.3.5.3 Reports of analyses of data from more than one study

Examples of reports that would be found in this section include: a report of a formal meta-analysis or extensive exploratory analysis of efficacy to determine an overall estimate of effect size in all patients and/or in specific subpopulations, and a report of an integrated analysis of safety that assesses such factors as the adequacy of the safety database, estimates of event rates, and safety with respect to variables such as dose, demographics, and concomitant medications.

A report of a detailed analysis of bridging, considering formal bridging studies, other relevant clinical studies, and other appropriate information (e.g., PK and PD information), should be placed in this section if the analysis is too lengthy for inclusion in the Clinical Summary.

5.3.5.4 Other study reports

This section can include:

- Reports of interim analyses of studies pertinent to the claimed indications;
- Reports of controlled safety studies not reported elsewhere; and,
- Reports of controlled or uncontrolled studies not related to the claimed indication.

5.3.6 Reports of Post-Marketing Experience

For products that are currently marketed, reports that summarize marketing experience (including all significant safety observations) should be included in this section.

5.3.7 Case Report Forms and Individual Patient Listings

Case report forms and individual patient data listings are subject to good clinical practice inspection where applicable.

5.4 Literature References

Copies of referenced documents, including important published articles, official meeting minutes, or other regulatory guidance or advice should be provided here. This includes copies of all references cited in the Clinical Overview, and copies of important references cited in the Clinical Summary or in the individual technical reports that were provided in Module 5.

Only one copy of each reference should be provided. Copies of references that are not included here should be immediately available upon request.

APPENDIX 1:

APPLICATION FORM FOR REGISTRATION

National Medicine Regulatory Authority, 120, Norris Canal Road, Sri Lanka

A. Type of application (check the box applicable)

New Application	
Periodic Re-registration	
Variation to existing marketing authorization (If selected, complete the information below.)	
▪ Previous registration number	
▪ Previous registration condition	
▪ Brief description of change intended	
▪ Reasons for variations	

B. Details on the product

1. Proprietary name (trade name)				
2. Approved generic name (s) (use INN if any)				
3. Standard claimed (BP, Ph.In, Ph. Eur., USP, IH, etc				
4. Strength(s) per dosage unit				
5. Dosage form				
6. Route of administration				
7. Shelf life (months)				
8. Storage condition				
9. Visual description				
10. Description of container closure				
11. Packaging and pack size				
12. Therapeutic category				
13. Expected schedule of the medicine (Please refer relevant section of the NMRA regulations)				
	Schedule 1			
	Schedule 2 A			
	Schedule 2 B			
	Schedule 2 C			
	Schedule 3			
14. Complete qualitative and quantitative composition (indicate per unit dosage form, e.g., per tablet, per 5ml, etc.) ▪ Add/delete as many rows and columns as needed.	Composition	Quantity	Function	Claimed standard

15. Complete qualitative and quantitative composition (indicate per batch in Kg, L, etc.) ▪ Add/delete as many rows and columns as needed.	Composition	Quantity	Function	Claimed standard
16. Statement of similarity and difference of clinical, bio-batch, stability, validation, and commercial batch sizes				

17. Regulatory situation in other country (Provide a list of countries in which this product has been granted a marketing authorization and the restrictions on sale or distribution, e.g., withdrawn from the market, etc.)	

C. Details on the applicant

1. Name	
2. Business address	
3. postal address	
4. Telephone number /Fax number	
5. E mail	
6. Web site	
7. Details	

F. Details on dossiers submitted with the application Section of dossier

	Module	**Annex, page number, etc.**
1	Module 1	
2	Module 2	
3	Module 3	
4	Module 4	
5	Module 5	

CERTIFICATION BY A RESPONSIBLE PERSON IN THE APPLICANT COMPANY

I, the undersigned, certify that all the information in the accompanying documentation concerning an application for a marketing authorization for;

1.	Proprietary name (trade name)	
2.	Approved generic name(s) (INN)	
3.	Strength(s) per dosage unit	
4.	Dosage form	
5.	Applicant	
6.	Manufacturer	

is correct and true, and reflects the total information available.

Signature	
Name	
Position in company	
Date:	

APPENDIX 2 :

REQUIREMENTS FOR RE-REGISTRATION

A product registration certificate is valid for five years. Therefore, an applicant is required to apply for re-registration within six months prior to the due date.
The application for reregistration should include:

1. Information and dossiers indicated in Module 1 of this Guideline.

2. Summary of the Annual Product Report (APR) for batches produced and marketed in Sri Lanka since the grant of marketing authorization. For the purpose of reregistration, the APR should include all batches produced over the prior five years and a product quality review should be submitted with the objective of verifying the consistency of the quality of the FPP and its manufacturing process.

Rejected batches should not be included in the analysis, but must be reported separately together with the reports of failure investigations, as indicated below.

3. Reviews should be conducted with not less than 10 consecutive batches manufactured over the period of the last 12 months or, where 10 batches were not manufactured in the last 12 months, not less than 25 consecutive batches manufactured over the period of the last 36 months, and should include at least:

1) Review of starting and primary packaging materials used in the FPP, especially those from new sources;
2) Tabulated review and statistical analysis of quality control and in-process control results;
3) Review of all batches that failed to meet established specification(s);
4) Review of all critical deviations or non-conformances and related investigations;
5) Review of all changes carried out to the processes or analytical methods;
6) Review of the results of the stability-monitoring program;
7) Review of all quality-related returns, complaints and recalls, including export- only medicinal products;
8) Review of the adequacy of previous corrective actions;
9) List of validated analytical and manufacturing procedures and their re-validation dates;
10) Summary of sterilization validation for components and assembly, where applicable;
11) Summary of recent media-fill validation exercises;
12) Conclusion of the Annual Product Review;

13) Commitment letter that prospective validation will be conducted in the future; and, the Protocol.

4. Tabular summary of any variations notified, accepted, and pending with the Authority since the grant of marketing authorization.

5. Copies of the current API and FPP specifications, duly signed and dated, including the test methods. The specifications should indicate the reference number, version number, effective date, and change history, if any.

6. Samples of actual products

APPENDIX 3:
SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the finished pharmaceutical product
2. Qualitative and quantitative composition
3. Pharmaceutical form
4. Clinical particulars

1. Therapeutic indications
2. Posology and method of administration

a. Children and adolescents (4 to 17 years of age)
b. General administration recommendations
c. Special dosing considerations in adults

3. Contraindications
4. Special warnings and special precautions for use
5. Interaction with other fpps and other forms of interaction
6. Use in Pregnancy and lactation
7. Undesirable effects [*See example below*.]
8. Overdose

5. Pharmacological properties

5.1 Pharmacodynamic properties

1. Pharmacotherapeutic group: {group}
2. ATC code:
3. Mechanism of action
4. Pharmacodynamic effects

- Adults
- Pediatric patients if recommended

5.2. Pharmacokinetic properties

1. Absorption
2. Distribution
3. Biotransformation

4. Elimination

5. Characteristics in patients

5.3. Preclinical safety data

Data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction

5. Pharmaceutical particulars

1. List of excipients

2. Incompatibilities

3. In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products. “This medicinal product must not be mixed with other medicinal products “

4. Shelf life

5. Special precautions for storage

6. Special precautions for usage / preparation before use . Ex:

- Products to be reconstituted -

Method of preparation, the diluent to be use and shelf-life after preparation

- Tablets –

Division of the tablet –state whether tablet can be divided or not

- Special equipment for use, administration or implantation
- Special precautions for disposal and other handling

19. REFERENCE LIST

1. WHO Technical Report Series, No. 863
2. WHO Technical Report Series, Nos. 902
3. WHO Technical Report Series, Nos.908
4. WHO Technical Report Series, No. 929
5. WHO Technical Report Series, No. 943
6. WHO Technical Report Series, No. 953
7. ICH Guidelines Q1A, Q1B, Q1C, Q1D, Q1E, Q3A, Q3B, Q3C, Q5C, Q6A, and Q6B
8. ICH Guidelines Q1A, Q1B, Q1D, Q1E, Q2

20. FEEDBACK

22.1Staff and customers may provide feedback about this document by emailing info@nmra.gov.lk

GUIDELINE FOR REGISTRATION OF MEDICAL DEVICES IN SRI LANKA

Cosmetic Devices and Drug Regulatory Authority (CDDA)
No. 120, Norris Canal Road,
Colombo 10,
Sri Lanka

November 2011

PREFACE

This document is intended to provide general guidance and will assist importers and local manufactures of medical devices in the submission of applications for product registration.

1.0 INTRODUCTION

1.1.PURPOSE

This document is meant to provide general guidance and assist to medical device importers and local manufacturers when submitting applications for regulatory approval to the CDDA.

1.2 BACKGROUND

In Sri Lanka "The Cosmetics Devices and Drug Act No.27 of 1980 and its subsequent amendments are the legislative framework to regulate Cosmetics, Devices and Drugs.

In case of devices registration , individual products are registered separately after evaluating each product for following parameters i.e. quality, safety, effectiveness and durability and will issues a 'marketing authorization', or licence.. For imported medical devices the registration application should be submitted through the local agent representing the manufacturer in Sri Lanka to the CDDA.

Local manufacturing plants are also licensed directly by CDDA. Regarding manufacturing, the main focus is on the certificate of good manufacturing practices issued by the regulatory authority of manufacturing country.

According to the regulations, documents required for registration of medical devices should be submitted conforming to the form A Schedule 1 Regulation 4 (3). [Annex 1]

1.3 SCOPE

This document applies for all medical devices. The government of Sri Lanka (CDDA) regulates the manufacture, sale and importation of devices by requiring that all devices be registered before they can be manufactured, supplied, distributed or sold.

1.4 DEFINITION OF A DEVICE

"Device" means any article, instrument, apparatus or contrivance, including any component, part of accessory thereof;, manufactured or sold for use in,

- the diagnosis, treatment, mitigation or prevention of disease, disorder or abnormal physical state or the symptoms thereof, in man or animal,
- restoring, correcting or modifying a body function or the body structure of man or animal,
- the diagnosis of pregnancy in human beings or animals, or
- the care of human beings or animals during pregnancy and at and after birth of the off-spring, including care of the off-spring and includes a contraceptive device but does not include a drug

2.0 REGISTERING PROCEEDURE OF DEVICES

Persons who import or manufacture medical devices or have products imported or manufactured on their behalf are responsible for applying to the Cosmetics, Devices & Drug Regulatory Authority (CDDA) to get pre marketing approval. The applicant shall be responsible for the product and all information supplied in support of his application for registration of the product.

2.1 Responsibilities of a applicant

The applicant/ registration holder either manufacturer or importer must in writing declare that they are responsible for ensuring safety, quality & effectiveness of the registered devices and that the product complies with all existing regulations and specifications (standards)

Responsibilities include

- Responsible for product and all the information supplied in support of his application for registration of product and for updating any information relevant to the product
- having effective procedure for handling any adverse effects that may occur with the product in use.
- Execute suitable quality control
- Ensuring appropriate packaging material is used to guarantee quality of the product

2.2 The procedure of registration of devices is as follows

2.2.1 Applying for a sample licence

In order to apply for the sample license the applicant should submit

- Request letter for registration
- Business registration certificate BR(1)
- Authorization letter issued by the manufacturer by appointing the applicant as the local agent for the relevant products

Authorization letter should be addressed to director CDDA & it should be signed by the General manager or CEO of the manufacturing company with the name & designation. In addition the information regarding other agents in other countries are preferred.

- Copy of free sale certificate

If above documents are in order the applicant will receive payment letter from the receiving point of CDDA & then he should have to make relevant payments to the shroff counter at the Ministry of Health (MOH). Along with the above relevant documents yellow receipt which is issued by MOH should be submitted to the CDDA receiving point after making the date stamped on the receipt.

Then at the receiving point the application will be entered in to a register.

The sample licence will be issued in three copies which is valid for period of one year from the issuing date & applicant will be able to collect it from the receiving point. (Another copy will be attached to the dossier)

Then local agent can submit the dossier with samples.

2.2.2 Submission of application

The application need following requirements on submission

- application should be in a box file
- three separate files are to be prepared
- First page should contain following details
  Eg. approved name, brand name, Manufacturer's details, impoter's details.
- application should be numbered inserting polio numbers from top to bottom & bottom to top as well

(1). Basic requirements

- Index
- Acknowledgement
- Copy of sample import licence
- Schedule I Form A Regulation 4 (3)

I. Name and address of the applicant , manufacturer and importer

II. Name of the Device , brand name (if any), official or approved name

III. A Certificate from the health authorities of the country in which it is produced confirming that the device is in use there and the period of use and if not, reasons for not marketing it in the country of the manufacture (Free sale certificate) - original or copy of a free sale certificate which is attested by a FDA/ Medical device control agency / Sri Lankan embassy or foreign ministry is acceptable original attested by D/ CDDA

IV. List of countries with documents to prove registration status in other countries eg. Foreign country registration certificate

V. Fully packed samples of the devices

The applicant should be able to submit at least two samples from commercial batches in order to send for external evaluators

eg. For sterile products, Single user products

Two samples are also be submitted for instruments & apparatus

In case of machineries & highly expensive devices the local agent should be in a position to demonstrate description of those machines to external evaluators when they require to do so.

(The applications without relevant samples are not be acceptable & will not be sent for external evaluators)

VI. Sample of the label(s) with inner & outer cartons

Product catalogue to aid the identification of the product

Lot no., Manufacture date , Expiry date, manufacturers name address ,country of origin should be indicated on the label

- Schedule I form B Name, designation & signature of the applicant

(2) Other Requirements

The following documents should be submitted in addition to the basic documents / details above mentioned where necessary / if available

1) Test reports should be submitted for the below mentioned products

- Independent analytical certificates from Industrial Technology Institute (ITI) or govt. accreted laboratory in Sri Lanka (original report should be submitted) for products which are directly in contact with the blood stream such as disposable syringes, disposable needles, IV cannulas IV catheters etc. Test reports are to be submitted according to pharmacopeial standards
- Standardization reports from Sri Lanka Standard Institution (SLSI) are needed for certain items

  eg. Plasters, gauze, feeding bottles, sanitary Napkins, bandages, latex condoms, Surgical gloves etc.
- ISO certification in order to access the design, development, manufacturing as well as for post marketing monitoring of safety and performance of the manufacturer.
- CE accreditation in order to prove the free sale within the Europian Union

2) Following requirements should be fullfilled for Absorbable sutures with the application.

- All the samples of absorbable sutures will be kept at the CDDA for six (6) months before sending for evaluation to the relevant consultant.
- Details of the raw material sources, purchasing details should be provided.
- Analytical certificate of the finished product according to relevant standards should be provided from an Independent Laboratory as well as from manufacturer.
- Stability data for entire shelf life of the finished products should be provided.

3) Where necessary certificate of approval from relevant authorities should be provided.

eg: - For radiation emitting devices approval obtained from Atomic energy Authority of Sri Lanka

- Certification from the relevant health authority of the country of manufacturer that the product is free from BSE (Bovine Spongiform Encephalopathy) should be obtained for animal derived products eg: Surgical Catgut

4) Instructions for use should be in three languages English, Sinhala & Tamil for relevant products such as Glucometer, Hearing Aids, Ear and Forehead Thermometers should be submitted whenever necessary.

5) For High cost cardiac devices relevant information according to the "Guidelines for registration of Cardiac devices/ stents" dated 28th Feb 2009 prepared by the committee appointed to overlook the registration of High Cost Cardiac Devices (HCCD) should be submitted. (A copy be to be included in web site)

6) For Borderline devices with therapeutic claims relevant clinical trial data should be submitted.

7) Other special requirements would be considered on case by case basis and as decided by the Medical Device Evaluation Sub Committee (MDESC) of the CDDA.

(3) Labels & Product information leaflets

Labelling requirements

The container of every device imported, manufactured, processed or packed locally or sold or exposed for sale shall have labels bearing the following information clearly.

1) The approved name (official name) & Brand name (Trade name). Where standards are available labels more should be produced accordingly.
   eg: Absorbent Cotton wool BP (British Pharmacopoeia)
2) The intended purpose of use.
3) Any special storage conditions that may be necessary
4) Any warning and precautions that may be necessary
5) The date of manufacturer and date of expiry where applicable; (An indication of the date until which the device may safely be used expressed as the year and the month
   (eg. single –use disposable devices)
6) The batch or lot number assigned by the manufacturer ;
7) The name and address of the manufacturer including country of manufacturing;

8) Adequate directions for use of the device
9) For imported devices, the label to the outer packaging to have the name and address of the local importer
10) Sufficient details for the user to identify the device, or where relevant, the contents of any packing.
11) An indication that the manufacturer for single use has specified the device "For single use only".
12) Date of manufacture & Date of expiry, any special storage and/ or handling conditions on the external packaging condition
13) When a medical device is manufactured by a source other than the principal manufacturer (loan/ contract manufacturer etc.), the label should clearly identify the name and address of such manufacturer as follows. "Manufactured by …… For ……" and the country of origin should be clearly stated in the label.
14) If a particular medical device is distributed by a source other than the principal manufacturer, the label must clearly identify the name and address including the country of origin of the distributor as follows. "Manufactured by ……. Distributed by……".
15) In addition to the above, any other requirements for labeling that may be mandated from time to time by the CDDA shall be complied with.

Product information leaflet

1) The performance intended by the manufacturer and undesirable side- effects.
2) The information needed to verify the device is properly installed and can operate correctly and safely. Replacement of consumable components, and calibration needed to ensure that the device operates properly and safely during its intended life.
3) Detail of any further treatment or handling needed before the device can be used (Eg. sterilization, final assembly, calibration etc.)where applicable should be indicated.
4) An indication that the device is sterile and also necessary instructions in the event of damage to sterile packaging and, where appropriate, description of methods of re- sterilization. /or whether it cannot be re- sterilized /or cannot be re-used by sterilization
5) If the device is to be installed with or connected to other medical devices or equipment in order to operate as required for its intended purpose.

6) If the device is implantable, information regarding any particular risk in connection with its implantation.
7) Information regarding the risks of reciprocal interference posed by the reasonably foreseeable presence of the device during specific investigations or treatment
   (Eg. Electrical interference from electro – surgical devices or magnetic field interference from magnetic resonance imagers).
8) If the device is reusable, information on the appropriate processes to allow reuse, including, disinfections, packaging and, where appropriate, the method of re-sterilization and any restriction on the number of re-uses.
9) Where device are supplied with the intention that they be sterilized before use, the instruction for cleaning and sterilization should be such that, if correctly followed, the device will "still comply with" the essential principles of safety and performance of medical devices".
10) If the device emits radiation for medical purposes, details of the nature, Type, intensity and distribution of this radiation.
11) The instructions for use should also include, where appropriate, details allowing the medical staff to brief the patient on any contra indications, warnings and any precautions to be taken. These details should cover in particular:
   (a) Precautions to be taken in the event of changes is performance of the device.
   (b) Precautions to be taken as regards exposure, in reasonably foreseeable environmental conditions, to magnetic fields, external electrical influences, electrostatic discharge, pressure or variations in pressure, acceleration, thermal ignition sources, proximity to other devices, etc.
12) Adequate information regarding any medical product or which the device in question is designed to administer, including any limitations in the choice of substances to be delivered.
13) Precautions to be taken against any special, unusual risks related to the disposal of the device.
14) Any medical substances incorporated into the device as an integral part of the device.
15) Degree of accuracy claimed for devices with a measuring function.
16) Any requirement for special facilities, or special training, or particular qualifications of the device

2.3 Multiple applications

(1) Separate application to be submitted when a medical device consists of different constituents/ components. Each and every component of that system is registered separately.

eg: (i) Orthopedic system - separate applications should be produced for bone plates, nails, pins, screws

(ii) Dental appliances

(2) A medical device although the manufacturing process is same and share a common intended purpose is registered separately.

eg: (i) Condoms with different colour, size, texture

(ii) Syringes with different volumes

(iii) CV catheters, haemodialysis instruments, blood bags (for single, double and triple)

(3) In vitro diagnostic devices that consist of reagents or article intended to be used in combination to complete a specific intended purpose is registered as a group

eg: Hematology analyzer with standards, programme and reagents

Or as separately

eg: Blood grouping reagent, blood glucose monitoring system with component

A medical device although the manufacturing process and share

(4) A medical device consisting a collection of devices and has a common intended purpose is registered as a group.

eg: (i) Electro surgical unit with standard accessories (electrodes, electrode holders, leads, Plates, plug adopter)

(ii) Centrifuge and standard accessories

(iii) Nebualizer system

2.4. File submission procedure

- Application should be submitted to the pharmacist at the receiving point and he will issue processing fees payment letter & applicant have to make the payments to the shroff counter of the ministry of health. From the shroff counter yellow receipt will be issued and it should be attached to the dossier after making date stamped.

- Complete application should be submitted to the pharmacist at the receiving point with samples where the dossier will be cross checked with a checklist by the pharmacist & will decide whether the dossier is in order.

- Pharmacist will enter the dossier into a register with a serial no. (DVR no). & the acknowledgement will be given back to the local agent with DVR no., signature & date stamp.

Local agent can follow up on dossier with the DVR no. hereafter.

Special Requirements

Special requirements, which apply only to some medical devices,

- Chemical, physical and biological properties of the medical device
- Minimization of risk of infection and microbial contamination to a patient, a user or any other person
- Construction and environmental properties of the device should be safe
- Medical devices with a measuring function should provide accurate precise and stable measurements
- Protection against radiation of the patient user or any other person
- Medical devices connected to or equipped with an energy source must be designed and produced in such a way that it ensures the performance, reliability and repeatability of the system and risks associated with a single faulty condition are minimized.

2.5. Processing of evaluation

Applications are subjected to basic evaluations by the internal evaluators. According to basic evaluation if dossier is unsatisfactory those applications will be rejected. If the application is in order, the name will be sent to external evaluators with samples for clinical evaluation.

With the external evaluators report the application will be submitted to MDESC for discussion & to get the decision. According to the committee's recommendation & approval the application will be granted provisional/full registration. If the application is failed with in the process the local agent can appeal for the registration.

2.5.1 Validity of registration

- Full registration

Full registration of devices will be valid for a period of five (5) years and is specified in the certificate. Renewal of registration is to be done every five yearly.

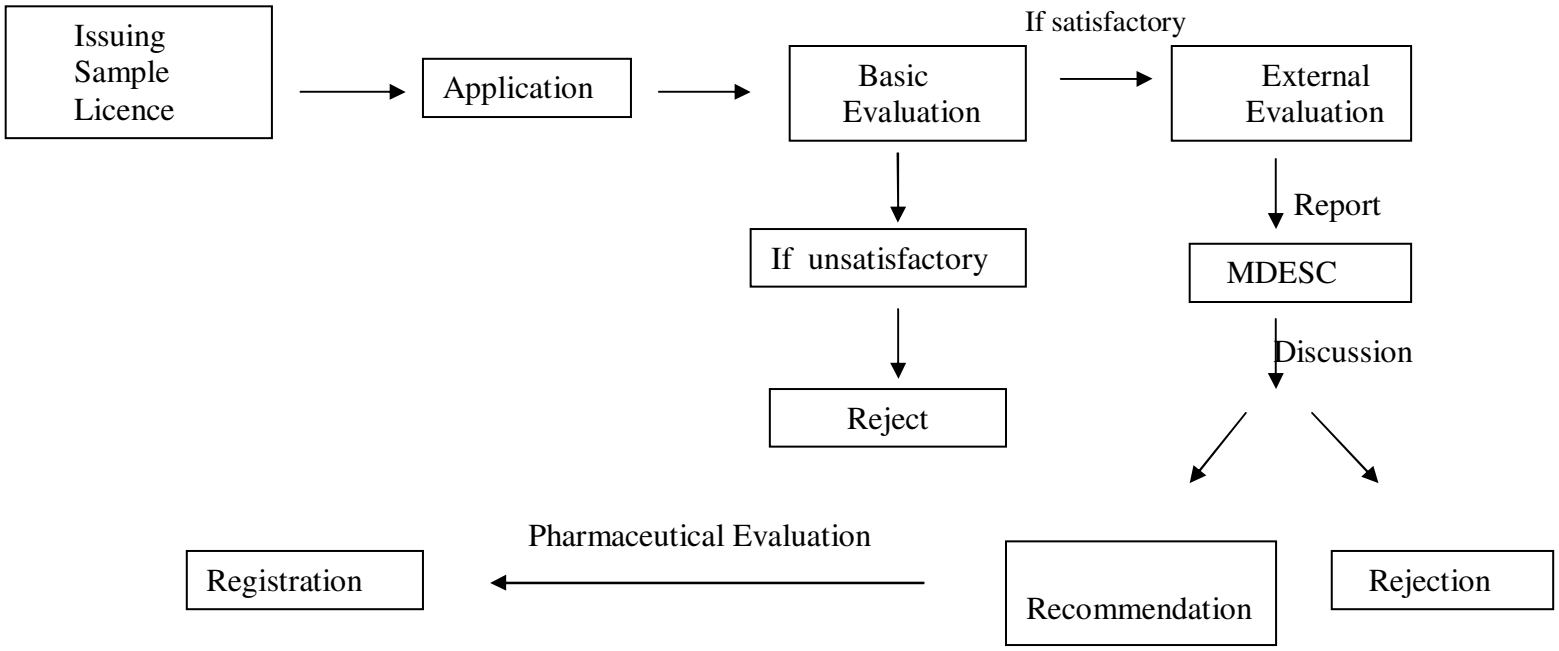
- Provisional Registration

Under certain circumstances provisional registration will be granted for a period of one year such as ;

- New device
- New specifications of a device
- New manufacturer
- In case of agency transfers
- Products which have been suspended due to quality problems
- Applications that do not provide required documentation as outlined above for registration of a devices

These registration certificates will be issued by the CDDA in three copies. One copy will be given to local agent, another copy will be attached to dossier & other copy will be filed in a CDDA

REGISTRATION OF MEDICAL DEVICES



2.5 Applying for import licence

- After applicant has obtained a registration, with the copy of registration certificate & request letter the applicant can apply for import licence.
- The payment should be made into shroff counter of the MOH and yellow receipt should be submitted after making date stamp with the above documents to the receiving point of the CDDA. The import licence will be issued in three copies. One copy will be issued to applicant , another copy will be attached to the application and other copy will be filed in CDDA.
- Import licence should be renewed every year