الإدارة المركزية للرقابة الدوائية

وحدة برامج الإعتماد

دليل برنامج
إعتماد هيئة الدواء المصرية
بمصانع شركات الأدوية لمعامل مراقبة الجودة

لسنة ٢٠٢١

الكود: **EDREX:GL.CADC.001**
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تاريخ التفعيل: **6/3/2021**

جدول المحتويات

١- المقدمة

يهدف البرنامج الي الإرتقاء بمستوى صناعة الدواء والأداء الرقابى بمعامل مراقبة الجودة بشركات الأدوية وذلك من خلال منح هيئة الدواء المصرية شهادة إعتماد معامل مراقبةالجودة بمصانع شركات الأدوية وذلك لبعض المستحضرات الصيدلية البشرية طبقا للمعايير التى تضعها هيئة الدواء المصرية

٢- النطاق

- التشغيلات الخاصة بالسحب العشوائى .
- التشغيلات الإنتاجية الثانية والثالثة .
- التشغيلات الحاصلة على موافقة إضافة أو تغيير مورد أو نقل تصنيع

٣- الاختصارات :لايوجد

٤- التعريفات:لا يوجد

٥- الموضوع الرئيسي:

٥.١ مميزات البرنامج

- فحص ملف المستحضر مرة واحدة عند التقدم للحصول على الشهادة والإعفاء من الفحص والإستيفاء بكل مرة يتم بها سحب المستحضر.
- إعتماد نتائج تحليل معامل شركات الأدوية دون التحليل بمعامل الإدارة المركزية للرقابة الدوائية للمستحضرات المدرجة بالجدول المرفق بشهادة الإعتماد.
- تمنح الشركة شهادة إعتماد (سارية لمدة عام وتجدد) للمستحضرات التى تم إعتمادها.

٥.٢. مميزات إضافية

طبقاً للقواعد التالية

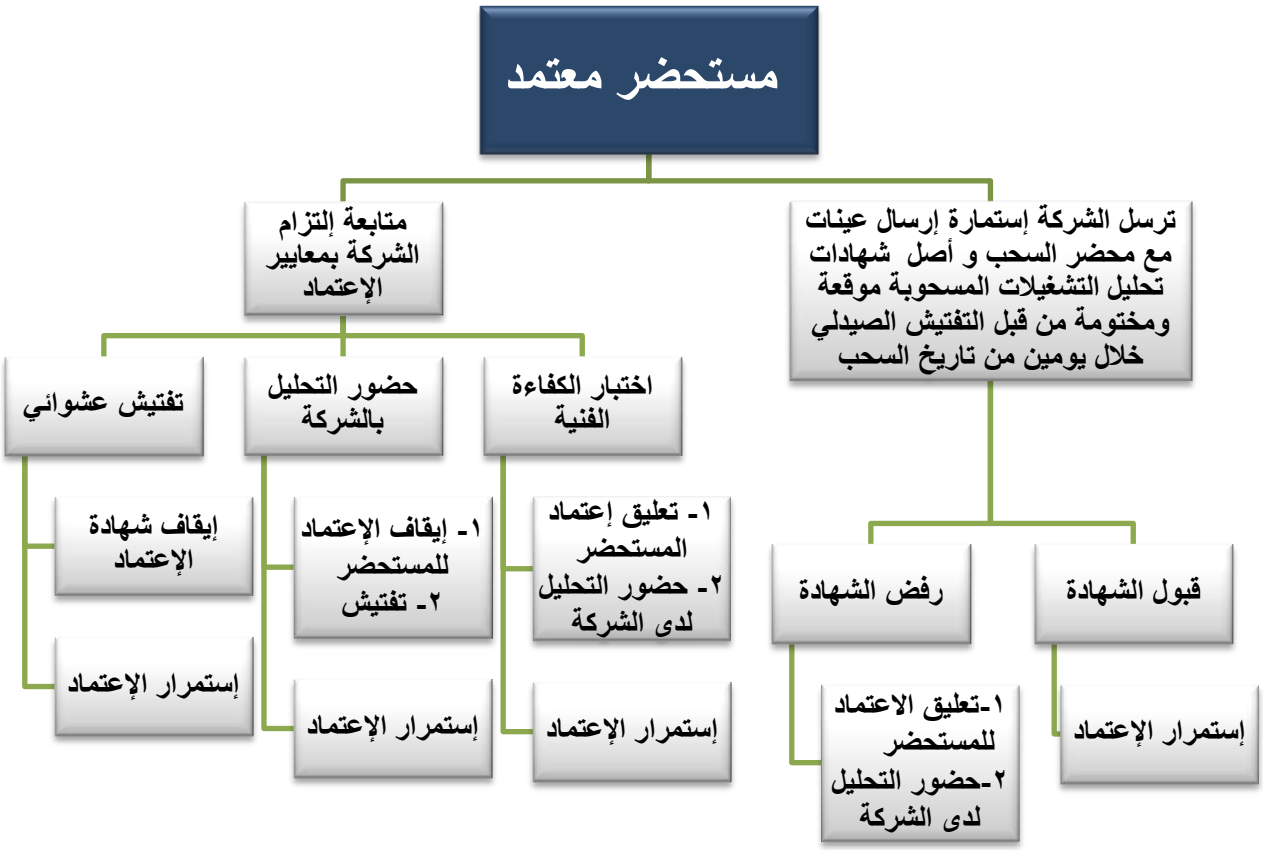
م	نوع الخدمة	مميزات إضافية
١	طلب إعتماد لعدد من خمس إلى تسعة مستحضرات مسجلة "سحب عشوائى".	لا يوجد
٢	طلب إعتماد لعدد "من ١٠ إلى ١٤" مستحضرات مسجلة "سحب عشوائى" ، مع السماح بتقديم طلبات إعتماد لنفس المستحضرات فى حال حصولها على موافقة إضافة أو تغير مورد .	يقابله طلب إعتماد مستحضرين "تشغيلة إنتاجية ثانية وثالثة أو تشغيلة حاصلة على موافقة إضافة أوتغيير مورد أو نقل تصنيع".
٣	طلب إعتماد لعدد من "١٥ إلى ١٩ " مستحضر مسجل – "سحب عشوائى" ، مع السماح بتقديم طلبات إعتماد لنفس المستحضرات فى حال حصولها على موافقة إضافة أو تغير مورد.	يقابله طلب إعتماد أربعة مستحضرات "تشغيلة إنتاجية ثانية وثالثة أو تشغيلة حاصلة على موافقة إضافة أوتغيير مورد أو نقل تصنيع".
٤	طلب إعتماد لكل عشرين مستحضر مسجل " سحب عشوائى " ، مع السماح بتقديم طلبات إعتماد لنفس المستحضرات فى حال حصولها على موافقة إضافة أو تغير مورد .	يقابله طلب إعتماد ستة مستحضرات "تشغيلة إنتاجية ثانية وثالثة أو تشغيلة حاصلة على موافقة إضافة أوتغيير مورد أو نقل تصنيع".

٥.٣ إجراءات ماقبل الإعتماد

الاجراء	جهة التنفيذ
تقوم الشركة بحجز موعد لسداد رسوم القيد	الشركة
ملء نموذج التقديم و رفع مستندات ملحق ١ بعد سداد رسوم القيد	الشركة
يتم الرد على الشركة بالقبول أو الرفض (ثلاث ايام عمل) [1]	الادارة المركزية للرقابة الدوائية
سداد رسوم التقدم للحصول على الشهادة مع رفع مستندات ملحق ٢ (ثلاث أيام عمل) [2]	الشركة
دراسة المستندات المقدمة و مراسلة الشركة لحين الإستيفاء (خمسة عشر يوم عمل)[3]	الادارة المركزية للرقابة الدوائية
تحديد موعد لزيارة معامل الشركة للقيام بالتفتيش (فترة الزيارة لا تتجاوز خمسة أيام عمل) [٤]	الادارة المركزية للرقابة الدوائية
إرسال تقرير بنتائج التفتيش للشركة (خمسة أيام عمل)	الادارة المركزية للرقابة الدوائية
إرسال الشركة خطة للإجراءات التصحيحية المطلوبة (خمسة أيام عمل) [٥]	الشركة
دراسة الخطة التصحيحية المقدمة و تحديد موعد زيارة أخرى ان لزم الأمر(ثلاث أيام عمل) [٦]	الادارة المركزية للرقابة الدوائية
يتم إعداد التقرير النهائي للإعتماد ، مع التوصية سواء بالقبول أو بالرفض (عشرة أيام عمل)	الادارة المركزية للرقابة الدوائية
يتم إصدار الشهادة مرفق معها تقرير موضح به أسماء المستحضرات الحاصلة على الإعتماد	الادارة المركزية للرقابة الدوائية

١. فى حال وجود طلب استكمال تقوم الشركة بإرساله فى خلال يومين ويتم الرد على الشركة فى خلال يومين.
٢. المستندات المطلوب تقديمها ورقيا هي: أصل إيصال سداد مقابل خدمة الحصول على شهادة الإعتماد / أصل خطابات التفويض المذكورة بنموذج التقديم / أصل نموذج التقديم موقع من الشخص المفوض.
٣. تمنح الشركة مهلتين إضافيتين لاستكمال كافة المتطلبات بملحق ٢ علي ان تقوم الشركة بالرد خلال يومين ويتم الرد علي الشركة خلال يومين لكل مدة
٤. ترسل الشركة خطاب تاكيد للزيارة خلال فتره اقصاها يومين
٥. المدي الزمني لتصحيح اي بند بالخطة التصحيحية لايزيد عن شهر
٦. تمنح الشركة مهلتين إضافيتين لإنهاء كافة الإجراءات التصحيحية المطلوبة وفى حال عدم إستيفاء المتطلبات يعتبر الطلب كأن لم يكن

٥.٤. إجراءات ما بعد الإعتماد



٥.٥. امتيازات التجديد

- **عند حصول الشركة على نسبة ٩٥% فأكثر من معايير المتابعة**

تمنح الشركة شهادة إعتماد سارية لمدة ثلاث سنوات مع سداد الشركة رسوم تجديد المستحضرات سنويا طبقا لقائمة المستحضرات المقدمة للتجديد .

يحق للشركة طلب إعتماد مستحضرأخر(ثاني و ثالث تشغيلة إنتاجية وحاصلة على إضافة أو تغيير مورد أو نقل تصنيع) بالإضافة إلى ما هو موضح بالجدول الخاص بأعداد المستحضرات المقدمة للإعتماد.

- **عند حصول الشركة على نسبة (٩٠% - ٩٥%) من معايير المتابعة**

تمنح للشركة طلب إعتماد مستحضر أخر (ثاني و ثالث تشغيلة وحاصل على إضافة أوتغيير مورد أو نقل تصنيع) بالإضافة لما هو موضح بالجدول الخاص بأعداد المستحضرات المقدمة للإعتماد.

٥.٦. ضوابط التحديث

- فى حال رغبة الشركة فى تحديث طرق تحليل بعد حصولها على الإعتماد لابد من إخطار الهيئة أولا ليتم دراسة الطريقة المحدثة و إعادة التقييم إن لزم الأمر .

- تقوم لجنة الإعتماد بالرد على الشركة فى خلال مدة زمنية لا تتجاوز عشرة أيام من تاريخ إرسال الشركة للطلب .

٥.٧. تجديد الإعتماد

يتم إتباع نفس الخطوات و يتم تقييم أداء الشركات لتجديد الإعتماد طبقا لنظام النقاط الاتي

المعيار	درجة التقييم
إلتزام الشركة بالمدد الزمنية الممنوحة لتنفيذ خطوات الحصول على الإعتماد.	١٠
تعاون ممثلي الشركة مع فريق التقييم أثناء زيارات التقييم أو ممثلي الإدارة المركزية للرقابة الدوائية أثناء التحليل لدى الشركة عند الضرورة .	١٠
نقاط التقييم التي حصلت عليها معامل مراقبة الجودة بالشركة طبقا للمعايير المطلوبة خلال مجمل زيارات التقييم عند الحصول وأثناء سريان شهادة الإعتماد .	٤٠
عدم حدوث تعليق مؤقت لإعتماد مستحضرأو أكثرخلال فترة الإعتماد .	١٠
عدم حدوث إيقاف مستحضرأو أكثرخلال فترة الإعتماد	٢٠
درجة إجتياز إختبار الكفاءة الفنية PT (e.g.z score)	١٠
المجموع	**١٠٠**

يمنح معمل مراقبة الجودة بالشركة ٥ نقاط إضافية في حال حصوله على إعتماد طبقا للمواصفة الدولية 17025:2017 أو مواصفة مكافئة.

لا يتم الموافقة علي تجديد الإعتماد في حال حصول الشركة علي نسبة اقل من ٨٠%.

٥.٨ مقابل الخدمة

الخدمة	مقابل الخدمة
طلب الحصول / التجديد لشهادة الإعتماد	خمسة آلاف جنيها مصريا(5000 LE)
طلب إعتماد لمستحضر مسجل (سحب عشوائى)	عشرة آلاف جنيها مصريا(10000 LE)
طلب إعتماد لمستحضر (تشغيلة إنتاجية ثانية و ثالثة)	عشرون ألف جنيها مصريا(20000 LE)
طلب إعتماد لمستحضر حاصل على موافقة متغيرات نقل تصنيع	ثلاثون ألف جنيها مصريا(30000 LE)
طلب إعتماد لمستحضر حاصل على موافقة إضافة أو تغيير مورد (لكل مورد)	ثلاثون ألف جنيها مصريا(30000 LE)
إعتماد نتائج تحليل كل تشغيلة إنتاجية	ألفان جنيها مصريا(2000 LE)
طلب تجديد إعتماد مستحضر مدرج بالشهادة سنويا	عشرة آلاف جنيها مصريا(10000 LE)

٥.٩. الشروط العامة والأحكام

١ – الشركات المنوط بها التقدم للبرنامج هى شركات الأدوية البشرية المالكة لمصنع بجمهورية مصر العربية.

٢ – الحد الأدنى للتقدم للبرنامج هو خمسة مستحضرات مسجلة (سحب عشوائى).

٣ – يتم تحليل التشغيلة التجريبية والتشغيلة الإنتاجية الأولى الخاصة بشعبة التسجيل بمعامل الإدارة المركزية للرقابة الدوائية طبقا لما هو متبع من إجراءات و لا تخضع لمقترح الإعتماد.

٤ – تعتبر الشهادة الممنوحة من الهيئة حق لمعامل الرقابة على الجودة بالشركة وحدها دون غيرها في تحليل العينات المذكورة بالشهادة ، ولا يحق للشركة إستخدام هذه الشهادة في تحليل عينات أو إصدار تقارير للغير.

٥ – يتم فحص ملفات المستحضرات المقدمة للإعتماد طبقا لقواعد الفحص المتبعة بالإدارة المركزية للرقابة الدوائية.

٦ – تلتزم الشركة بتوفير كافة المواد الخام الفعالة وغير الفعالة اللازمة لإجراء اختبار الكفاءة الفنية طوال فترة سريان الشهادة و تقديمها عند الطلب مرفقا بها البيانات الموضحة بمرفق ٢.

٧ – تلتزم الشركة بالإحتفاظ بالعينات المحرزه لحين صدور المطابقة وجميع نتائج التحليل:

- Raw data with work sheets and audit trail
- Pyrogen test and microbiological analysis results as per attachment 1

٨- في حال تجاوز الشركة المدد الزمنية المحددة لتنفيذ أى إجراء أومتطلب يعتبر الطلب المقدم من الشركة كأن لم يكن ويحق للشركة التقدم بالتماس لرئيس الإدارة لمنح مدة إضافية ،ويتم دراسته و البت بقبوله من عدمه ،وفى حال الرفض يتحتم علي الشركة تقديم طلب جديد للحصول على شهادة الإعتماد.

٩- في حال رفض طلب الإعتماد أو إلغاء شهادة الإعتماد يكون من حق الشركة إعادة التقدم بطلب جديد بعد مرور مدة لا تقل عن ستة أشهر من تاريخ الرفض أو الإلغاء مع سداد الرسوم المقررة.

١٠- فى حال تعليق أو إيقاف شهادة الإعتماد يتم التحليل بمعامل الإدارة المركزية للرقابة الدوائية.

١١- لا يحق للشركة إلغاء أى إختبار أثناء فترة سريان شهادة الإعتماد.

١٢- تلتزم الشركة بإخطار الإدارة المركزية للرقابة الدوائية فور حدوث أى تعديلات فى المستندات المقدمة وتقوم لجنة الإعتماد بالرد على الشركة فى خلال مدة زمنية لا تتجاوز عشرة أيام .

١٣- يحق للشركة التقدم بطلب إعتماد مستحضر مسجل (سحب عشوائى) إضافي أو أكثر خلال فترة سريان الشهادة علما بأنه سيتم التجديد لكافة المستحضرات سنوياً بالتاريخ المقرر لتجديد الشهادة وأن الإضافة لا تؤهل للحصول على أى مميزات إضافية.

١٤- فى حال رغبة الشركة بتجديد شهادة الإعتماد يتم تقديم الطلب خلال فترة زمنية لا تقل عن ثلاثة أشهر من تاريخ التجديد.

١٥- يتم تقييم أداء الشركة سنوياً طبقا لنظام النقاط المعلن لاتخاذ القرار بالموافقة على تجديد الإعتماد من عدمه.

٥.١٠.الإيميل الرسمي لبرنامج الإعتماد

dc.labaccredit@edaegypt.gov.eg

٥.١١. الروابط الإلكترونية لبرنامج الإعتماد

نموذج خاص بحجز مواعيد دفع رسوم خدمة

- **Link of Appointment Form**
https://form.jotform.com/210411996777061

نموذج خاص بملحق رقم ١

- **EDA Accreditation, Annex 1**
https://forms.office.com/Pages/ResponsePage.aspx?id=CD8mgpydXU-0FU_0Fmn3_Z1FiDLBdgFGtEy1qLH13RlUM00zVlJMVUk3R0s0OVBYRjlRMVJFNFFaVi4u

نموذج خاص باستكمال ملحق ١

- **EDA Accreditation, Resubmission of Annex 1**
https://forms.office.com/Pages/ResponsePage.aspx?id=CD8mgpydXU-0FU_0Fmn3_Z1FiDLBdgFGtEy1qLH13RlUQ1dHQ0lPT00wOFpUTlVGMkVLRlcyRDlNTy4u

نموذج خاص بملحق٢

- **EDA Accreditation, Annex 2**
https://forms.office.com/Pages/ResponsePage.aspx?id=CD8mgpydXU-0FU_0Fmn3_Z1FiDLBdgFGtEy1qLH13RlUQ0VZSjhVVVFaNlpYM0FCWVRaSlZHR09NTC4u

- **EDA Accreditation, Resubmission of Annex 2 Version 1 2 الاستكمال الاول لملحق :**
https://forms.office.com/Pages/ResponsePage.aspx?id=CD8mgpydXU-0FU_0Fmn3_Z1FiDLBdgFGtEy1qLH13RlUMjhDSlpaME5TVURMMjJONE44RlRNV0hUMi4u
- **EDA Accreditation, Resubmission of Annex 2 Version 2 2 الاستكمال الثاني لملحق :**
https://forms.office.com/Pages/ResponsePage.aspx?id=CD8mgpydXU-0FU_0Fmn3_Z1FiDLBdgFGtEy1qLH13RlUQ1UwODFLVlA2UkU1VDYxSTdTU09EUUZGNS4u
- **EDA Accreditation, Annex of Updates نموذج خاص بالتحديثات**
https://forms.office.com/Pages/ResponsePage.aspx?id=CD8mgpydXU-0FU_0Fmn3_Z1FiDLBdgFGtEy1qLH13RlUOVUyUTRMTUFVVEgxSFdQMlVQTkk3VDM1US4u
- **EDA Accreditation, Visit Confirmation Letter نموذج خاص بتأكيد ميعاد الزيارة**
https://forms.office.com/Pages/ResponsePage.aspx?id=CD8mgpydXU-0FU_0Fmn3_Z1FiDLBdgFGtEy1qLH13RlUN0pTWktES1JQUTRPSVg1NDE1NURBNTdSNi4u
- **EDA Accreditation, CAPA Plan نموذج خاص بالخطة التصحيحية**
https://forms.office.com/Pages/ResponsePage.aspx?id=CD8mgpydXU-0FU_0Fmn3_Z1FiDLBdgFGtEy1qLH13RlUNTBNVkQxWUJHNFlKT0hYSVkyUU5PUzhXMC4u
- **EDA Accreditation, CAPA Plan Implementation 1 نموذج خاص بالتطبيق الأول لتعديلات الخطة التصحيحية:**
https://forms.office.com/Pages/ResponsePage.aspx?id=CD8mgpydXU-0FU_0Fmn3_Z1FiDLBdgFGtEy1qLH13RlURDNEUlY2TFFZUVQzTzFOTkEzQVpENDFXQS4u
- **EDA Accreditation, CAPA Plan Implementation 2 نموذج خاص بالتطبيق الثاني لتعديلات الخطة التصحيحية:**
https://forms.office.com/Pages/ResponsePage.aspx?id=CD8mgpydXU-0FU_0Fmn3_Z1FiDLBdgFGtEy1qLH13RlUNE81RzBOTTBHTzZSMU5ZUEVHQ1MyNjRJVC4u
- **EDA Accreditation, Attachments of Accredited Product - Results of Analysis نموذج خاص بمرفقات مستحضر معتمد و نتائج التحليل:**
https://forms.office.com/Pages/ResponsePage.aspx?id=CD8mgpydXU-0FU_0Fmn3_Z1FiDLBdgFGtEy1qLH13RlUOEpORFBTRFc3SVRSVlJNQkRZS0M3TTlKWC4u

٦- المراجع:

1. WHO good practices for pharmaceutical quality control laboratories, Annex 1, WHO TRS 957, 2010

2. WHO good practices for pharmaceutical microbiology laboratories, Annex 2, WHO TRS 961, 2011
3. WHO guidelines on quality risk management Annex 2, WHO TRS 981, 2013
4. Guidance on good data and record management practices, Annex 5, WHO TRS 996, ٢٠١٦.
5. WHO guidelines for preparing laboratory information file, Annex 13, WHO Technical Report Series 961, 2011.
6. EudraLex The Rules Governing Medicinal Products in the European Union Volume 4 EU Guidelines to Good Manufacturing Practice Medicinal Products for Human and Veterinary Use Annex 19 Reference and Retention Samples
7. General European OMCL Network (GEON) Quality Management system documents.
8. ICH quality guidelines.
9. Latest editions of pharmacopeias USP and BP, FDA guidance.

٧.المرفقات/ الملحقات:

٧.١ المرفقات:

-مرفق١: Pyrogen & microbiological analysis results data requirement

-مرفق ٢ :Proficiency testing requirements submission form

٧.٢ الملحقات:

-ملحق١ : المستندات المطلوب تقديمها

-ملحق2: المستندات المطلوب تقديمها

- ملحق3:Assessment check list

مرفق ١

Pyrogen & microbiological analysis results data requirement

Sterility & microbial count test

1) The sample size, sampling date, and the sampler name.
2) All equipment used in the test procedure i.e. incubators; autoclave, pH meter, balance, LAF and any other equipment used with their code numbers.
3) The batch numbers of media and any diluent or neutralizer used in the test, their preparation date, and sterilization cycle number.
4) The number of the SOP used to carry out the test.
5) The analyst and supervisor signature.

Antibiotics assays

1) Method reference.
2) Type & weight of antibiotic.
3) Type & volume of the solvent.
4) Dilution factor.
5) Concentrations used.
6) Standard antibiotic, potency and dilution.
7) Inhibition zone for cylinder plate method.
8) Absorbance for turbidimetric method.
9) Calculations.
10) Limits

Disinfectant efficacy

1) Type & concentration of compound.
2) Type of neutralizer.
3) Time interval for exposure.
4) Type & concentration of micro-organism.

Bacterial endotoxin test

Gel clot method

1) Sample name.
2) Sample batch number.
3) Testing date.
4) Reference.
5) Limit of endotoxin,Lysate (ג), Endotoxin: Ecoli.0113-Ecoli.055.B5, endotoxin batch no.
6) Lysate batch no., diluents used, diluent batch no., (LAL reagent water batch no. & exp.)
7) Certificates for LAL reagent & LAL reagent water.
8) PH.
9) Validation of lysate sensitivity.
10) Time in, Time out, Water bath temp.
11) Analyst name (name – signature), lab manager (name – signature).

Print out for other methods (if applicable) should be submitted in addition to the previous requirements.

مرفق 2

Proficiency testing requirements submission form

Product name / Registration no. :

Name of API:	B.N /lot no	Name of supplier (s)	Specification/ reference	Manufacture date	Retest /Expiry date	Storage conditions
1.						
2.						
3.						
4.						
5.						
6.						
7.						
8.						
9.						
10.						
Name of excipients :	B.N/ lot no	Name of supplier (s)	Specification/ reference	Manufacture date	Retest / Expiry date	Storage conditions
1.						
2.						
3.						
4.						
5.						
6.						
7.						
8.						
9.						
10.						

*Attached all certificates of analysis of the above API and excipients.
* Attached delegation letter as contact person.

Authorized contact person

Company Stamp

Signature:

Date:

ملحق 1

المستندات المطلوب تقديمها

١) رخصة سارية للمصنع.
٢) شهادة الإيزو 9001:2015 أو مواصفات مكافئة لتطبيق نظم الجودة.
٣) شهادة ممارسة التصنيع الجيد.
٤) تعهد من الشركة بتوافر كافة الأجهزة اللازمة لتحليل كافة الإختبارات للمستحضرات المطلوب إعتمادها.
٥) صورة إلكترونية من إيصال مقابل خدمة طلب الحصول على شهادة الإعتماد.
٦) صورة إلكترونية من خطابات التفويض المذكورة بنموذج التقديم.
٧) صورة إلكترونية من نموذج التقديم موقع من المفوض عن الشركة .

ملحق 2

١. دليل جودة محدث أو مستند مكافئ يحتوي على آخر إصدار من :

- الهيكل التنظيمي للمؤسسة التابع لها المعمل موضح بها موقع المعمل من هذا الهيكل وكذلك المخطط التنظيمي للمعمل (Lab Organogram)
- رسم لتخطيط معامل الرقابة (QC labs Layout)
- قائمة محدثة من الأجهزة والمواد القياسية المستخدمة في التحليل وأكواد تعريفها .

٢. الإجراءات والتعليمات والسياسات.

٣. Qualification of (microbiology lab, LAF and autoclaves)

٤. Microbiological method suitability test for each product

٥. Validation study of disinfectants used in microbiology lab

٦. صورة من عقود تصنيع لدى الغير في حال المستحضرات التي يتم تصنيعها للغير ويتم تحليلها بمعامل مراقبة الجودة بالشركة.

٧. صورة إيصال سداد مقابل الخدمة لطلب الإعتماد للمستحضرات المقدمة.

٨. المستندات اللازمة لفحص ملف تحليل مستحضر صيدلي كالتالى:

م	المستند
١	صورة من موافقة الإدارة المركزية علي تغيير المصنع أو نقل الملكية أو تغيير أسم الشركة عن ما تم التسجيل علية
٢	صورة التقرير التهائى و صورة من موافقة الإدارة المركزية علي أي تغيير طرأ علي المستحضر بعد إصدار التقرير النهائي
٣	صورة من مطابقة التشغيلة الأنتاجية الأولى فى حالة التقدم للحصول على إعتماد (تشغيلة ثانية و ثالثة)
٤	طريقة التحليل و طريقة التحقق كاملة
٥	شهادة المواصفات الخاصة بالمستحضر مطابقة للتقرير النهائى و /أو احدث فارماكوبيا (فى حالة اضافة أو تغيير مورد)
٦	في حال العينات المتطلب لها إختبارPyrogen test / Bacterial Endotoxin test لا بد من تسليم صورة من النشرة الداخلية .
٧	بيان التركيب المعتمد الذي يتم التصنيع عليه.

٨	تعهد الشركة بصحة كافة المستندات والطرق المقدمة وأنها الأحدث لدي الشركة
٩	صورة من أحدث إخطار تسجيل ساري موضح به أسماء أحدث موردين للمواد الخام

ملحق 3

Assessment check list

1. Organization and Management	
Clause	**Requirement**
1.1	The laboratory, or the organization of which it is part, should be an entity that is legally authorized to function and can be held legally responsible.
1.2	The laboratory should be organized and operate so as to meet the requirements laid down in these guidelines.
1.3a	The laboratory should have managerial and technical personnel with the authority and resources needed to carry out their duties and to identify the occurrence of departures from the quality management system or the procedures for performing tests and/or calibrations, validation and verification, and to initiate actions to prevent or minimize such departures; are not subject to commercial, political, financial and other
1.3b	The lab should have arrangements to ensure that its management and personnel not subject to commercial pressures or conflicts of interest that may adversely affect the quality of their work;
1.3 c	have a policy and procedure in place to ensure confidentiality of information contained in marketing authorizations, transfer of results or reports, and to protect data in archives (paper and electronic)
1.3 d	The lab should define, with the aid of organizational charts, the organization and management structure of the laboratory, its place in any parent organization and the relationships between management, technical operations, support services and the quality management system.
1.3 e	The lab should specify the responsibility, authority and interrelationships of all personnel who manage perform or verify work which affects the quality of the tests and/or calibrations, validations and verifications.
1.3 f	The lab should ensure the precise allocation of responsibilities, particularly in the designation of specific units for particular types of medicines.
1.3 g	The lab should nominate trained substitutes/deputies for key management and specialized

	scientific personnel.
1.3 h	The lab should provide adequate supervision of staff, including trainees, by persons familiar with the test and/or calibration, validation and verification methods and procedures, as well as their purpose and the assessment of the results.
1.3 i	The lab should have management which has overall responsibility for the technical operations and the provision of resources needed to ensure the required quality of laboratory operations
1.3 j	The lab should designate a member of staff as quality manager who irrespective of other duties he/she may have, will ensure compliance with the quality management system. The nominated quality manager should have direct access to the highest level of management at which decisions are taken on laboratory policies or resources.
1.3k	The lab should ensure adequate information flow between staff at all levels.
1.3 l	The lab should ensure the traceability of the sample from receipt, throughout the stages of testing, to the completion of the analytical test report.
1.3 m	The lab should maintain an up-to-date collection of all specifications and related documents (paper or electronic) used in the laboratory.
1.3 n	The lab should have appropriate safety procedures.
1.4 a	The laboratory should maintain a registry with receiving, distributing and supervising the consignment of the samples to the specific units.
1.4 b	The lab should maintain a registry with keeping records on all incoming samples and accompanying documents.
1.5	The lab must guarantee communication and coordination between the staff especially in large laboratories.

2. Quality Management System

Clause	Requirement
2.1	The lab should document the elements of its quality management system should be documented in a quality manual or equivalent documents, for the organization as a whole and/or for a laboratory within the organization.
2.2	The Quality Manual or equivalent documents should provide (as a minimum) the following policies: (a) a quality policy statement, including at least the following: (i) A statement of the laboratory management's intentions with respect to the standard of service it will provide, (ii) A commitment to establishing, implementing and maintaining an effective QMS, (iii)The laboratory management's commitment to good professional practice and quality of testing, calibration, validation and verification. (iv)A requirement that all personnel concerned with testing and calibration activities within the laboratory familiarize themselves with the documentation concerning quality and

(b) The structure of the laboratory (organizational chart).
(c) The operational and functional activities pertaining to quality, so that the extent and the limits of the responsibilities are clearly defined.
(d) outline of the structure of documentation used in the laboratory quality management system;
(e) The general internal quality management procedures;
(f) References to specific procedures for each test;
(g) Information on the appropriate qualifications, experience and competencies that personnel are required to possess.
(h) Information on initial and in-service training of staff.
(i) A policy for internal and external audit.
(j) A policy for implementing and verifying corrective and preventive actions.
(k) A policy for dealing with complaints.
(l) A policy for performing management reviews of the quality management system.
(m) A policy for selecting, establishing and approving analytical procedures.
(n) A policy for handling of OOS results.
(o) A policy for the employment of appropriate reference substances and reference materials.
(p) A policy to select service providers and suppliers.

2. Standard Operating Procedures

Clause	Requirement
2.3	The laboratory should establish, implement and maintain authorized written SOPs including, but not limited to, administrative and technical operations e.g. (a) personnel matters, including qualifications, training, clothing and hygiene; (b) change control; (c) internal audit; (d) dealing with complaints; (e) implementation and evaluation of corrective and preventive actions; (f) the purchase and receipt of materials and services; (g) the procurement, preparation and control of reference substances (h) the internal labeling, quarantine and storage of materials; (i) the qualification of equipment (j) the calibration of equipment; (k) preventive maintenance and verification of instruments and equipment; (l) sampling, if performed by the laboratory, and visual inspection; (m)the testing of samples with descriptions of the methods and equipment used; (n) the evaluation and investigation of atypical and OOS results; (o) validation of analytical procedures; (p) cleaning of laboratory facilities, including bench tops, equipment, work stations, clean

	rooms (aseptic suites) and glassware; (q) monitoring of environmental conditions, e.g. temperature and humidity; (r) monitoring storage conditions; (s) disposal of reagents and solvent samples; Safety measures
2.4	The activities of the laboratory should be systematically and periodically audited.
	The audits should be carried out by trained and qualified personnel, who are independent of the activity to be audited.
	Such audits should be recorded, together with details of any corrective and preventive action taken.
2.5	Management review of quality issues should be regularly undertaken (at least annually), including (a) Reports on audits or inspections and any follow-up required to correct any deficiencies. (b) the outcome of investigations carried out as a result of complaints received, doubtful (atypical) or aberrant results reported in collaborative trials and/or proficiency tests; and (b) Corrective actions applied and preventive actions introduced as a result of these investigations.

3. Documentation Control

Clause	Requirement
3.1	The laboratory should establish and maintain procedures to control and review all documents.
	A master list identifying the current version status and distribution of documents should be established and readily available.
3.2	The procedures should ensure that: (a) Each document, whether a technical or a quality document, has a unique identifier, version number and date of implementation. (b) Appropriate, authorized SOPs are available at the relevant locations, e.g. near instruments. (c) Documents are kept up to date and reviewed as required. (d) Any invalid document is removed and replaced with the authorized, revised document with immediate effect. (e) A revised history page includes references to the previous document. (f) Obsolete documents are retained in the archives to ensure traceability of the evolution of the procedures; any copies are destroyed. (g) All relevant staff are trained for the new and revised SOPs; and quality documentation,
3.3	The presence of change control system that ensures that: (a) During the review and revision procedure, documents are prepared by the original

initiator, or a person who performs the same function. Documents are reviewed, approved and authorized at the same management level as the original document.

(b) Staffs acknowledged, by a signature, that they are aware of applicable changes and their date of implementation.

4. Records	
Clause	**Requirement**
4.1	The laboratory should establish and maintain procedures for the collection of technical and scientific records
4.2	Records should include all original observations, including calculations and derived data, calibration, validation and verification records and final results of tests.
4.3	Quality and technical/scientific records (including analytical test reports, certificates of analysis and analytical worksheets) should be legible, readily retrievable, stored and retained within a suitable environment.
4.4	Quality Management records should include reports of both internal, external audits, management reviews, complaints and their investigations and records for the implementation and evaluation of CAPA corrective and preventive actions.

5. Data Processing Equipment and Data governance	
Clause	**Requirement**
5.2	For computers, automated tests or calibration equipment, and the collection, processing, recording, reporting, storage or retrieval of test and/or calibration data, the laboratory should ensure that: (a) Computer software developed by the user should be documented in sufficient detail and appropriately validated or verified as being suitable for use. (b) Procedures are established and implemented for protecting the integrity of data. Such procedures should include, but are not limited to, measures to ensure the integrity and confidentiality of data entry or collection and the storage, transmission and processing of data. In particular, electronic data should be protected from unauthorized access and an audit trail of any amendments should be maintained; (c) computers and automated equipment are maintained so as to function properly and are provided with the environmental and operating conditions necessary to ensure the integrity of test and calibration data; (d) Procedures are established and implemented for making, documenting and controlling changes to information stored in computerized systems. (e) Electronic data should be backed up at appropriate regular intervals according to a documented procedure. Backed-up data should be retrievable and stored in such a manner as to prevent data loss.

6. Personnel	
Clause	**Requirement**
6.1	The laboratory should have sufficient staff to perform its delegated functions and be suitably educated, skilled and trained.
6.2	The technical management should ensure the competence of all personnel operating specific equipment, instruments or other devices, who are performing tests and/or calibrations, validations or verifications. Their duties also involve the evaluation of results as well as signing analytical test reports and certificates of analysis.
6.3	Staff undergoing training should be appropriately supervised and should be assessed on completion of the training. Personnel performing specific tasks should be appropriately qualified in terms of their education, training and experience, as required.
6.4	Contract Staff" should be employed and be suitably assessed, evaluated and supervised.
6.5	The laboratory should maintain current job descriptions for all personnel involved in tests and/or calibrations, validations and verifications. The laboratory should also maintain records of all technical personnel, describing their qualifications, training and experience.
6.6	The laboratory should have appropriate managerial and technical personnel and be suitably qualified and experienced
7. Premises	
Clause	**Requirement**
7.1	The laboratory facilities should be of a suitable size and construction and to be designed to suit the functions and operations to be conducted in them.
7.2	The laboratory facilities should have adequate safety equipment located appropriately and measures should be in place to ensure good housekeeping.
	The laboratory should be equipped with adequate instruments and equipment, including work benches, work stations and fume hoods
7.3	The environmental conditions (lighting, energy sources, temperature, humidity and air pressure) should be appropriate, controlled and suitably monitored.
7.4	Special precautions should be taken to handle highly toxic substances, including genotoxic substances.
7.5	Archives should be provided to permit the secure storage and the retrieval of all documents and to which accesses should be restricted.
7.6	Procedures should be in place for the safe removal of types of waste including toxic waste reagents, samples and solvents.

7.9	The lab should have appropriate storage facilities.
7.10	There must be segregation of storage for samples, retained samples, reagents, laboratory accessories, reference substances and reference materials.
	The environment of storage areas should be controlled and monitored and access controlled
7.11	There should be appropriate safety procedures for the receipt and storage of toxic or flammable reagents.
	Segregation of the storage of flammable substances, fuming and concentrated acids and bases, volatile amines and other reagents.
7.12	Reagents subject to poison regulations or to the controls applied to narcotic and psychotropic substances should be suitably stored and controlled.
7.13	Gases also should be stored in a dedicated store

8. Equipment, instruments and other devices

Clause	Requirement
8.1	All equipment should be adapted, located, calibrated, qualified, verified and maintained as required.
8.2	The laboratory should have the required test equipment, instruments and other devices for the correct performance of the tests and/or calibrations, validations and verifications where sub-contracting of tests in other laboratories is conditional under EDA
8.3	All instrumentation, and other devices, must comply with the relevant standards, specifications, and qualification and requirements.

9. Contracts

Clause	Requirement
9.1	The laboratory shall have written procedures for the selection of suppliers of materials, and the provision of services, including maintenance and calibration.
9.2	The laboratory shall have documentary evidence for the evaluation of suppliers of critical consumables and services.
	The lab shall maintain an updated list of approved suppliers.
9.3	When a laboratory subcontracts work, which may include specific testing, it is to be done with organizations approved for the type of activity required. The laboratory is responsible for periodically assessing the competence of a contracted organization.
9.٤	There should be a written contract which clearly establishes the duties and responsibilities of each party, defines the contracted work and any technical arrangements made in connection with it. The contract should permit the laboratory to audit the facilities and competencies of the contracted organization and ensure the access of the laboratory to records and retained samples.
9.5	The contracted organization should not pass to a third party any work entrusted to it under contract without the laboratory's prior evaluation and approval of the arrangements.
9.6	The laboratory should maintain a register of all subcontractors that it uses and a record of the assessment of the competence of subcontractors.

10. Reagents	
GPPQCL Ref	**Requirement**
10.1-10.2	The laboratory shall ensure that all reagents and chemicals used in testing are of an appropriate quality and purchased from reputable, approved suppliers.
10.3	In the preparation of reagent solutions in the laboratory: (a) responsibility for this task should be clearly specified in the job description of the person assigned to carry it out. (b) Prescribed procedures should be used which are in accordance with published pharmacopoeial or other standards where available. Records should be kept of the preparation and standardization of volumetric solutions
10.4-10.6	All reagents, reagent solutions and volumetric solutions should clearly and appropriately labeled.
10.7	In the transportation and subdivision of reagents: (a) Whenever possible they should be transported in the original containers; and (b) When subdivision is necessary, clean containers should be used and appropriately labeled.
10.8	All reagent containers should be visually inspected to ensure that the seals are intact, both when they are delivered to the store and when they are distributed to the units.
10.9	Reagents that appear to have been tampered with should be rejected; however, this requirement may exceptionally be waived if the identity and purity of the reagent concerned can be confirmed by testing.
10.10	Water should be considered as a reagent. The appropriate grade for a specific test should be used as described in the pharmacopoeias or in an approved test when available.
10.11	Precautions should be taken to avoid contamination during its supply, storage and distribution.
10.12	The quality of the water should be verified regularly to ensure that the various grades of water meet the appropriate specifications
10.13	Stocks of reagents should be maintained in a store under the appropriate storage conditions
10.14	The person in charge of the store is responsible for looking after the storage facilities and

their inventory and for noting the expiry date of chemicals and reagents. Training may be needed in handling chemicals safely and with the necessary care.

11. Reference Substances and Reference Materials	
Clause	**Requirement**
11.1-11.2	The laboratory should use appropriate reference substances (RS) and reference materials (RM).
11.3	There should be an appropriate procedure to register and identify RSs.
11.4-11.7	All RSs should be identified on receipt which is quoted in the analytical report and work-sheet. RS register should be maintained with the following information available: (a) The identification number of the RS. (b) A precise description of the RS. (c) The source of the RS. (d) The date of receipt. (e) The batch designation or other identification code. (f) The intended use of the RS. (g) The location of the RS, and any special storage conditions. (h) Any further necessary information. (i) Expiry date or retest date. (j) Certificate. (k) In the case of secondary reference substances prepared and supplied by the manufacturer, the certificate of analysis.
11.8	A person should be nominated to be responsible for reference substances and reference materials.
11.10	In addition a file should be kept in which all information on the properties of each reference substance is entered including the safety data sheets.
11.11	For reference substances prepared in the laboratory, the file should include the results of all tests and verifications used to establish the reference substances and expiry date or retest date; these should be signed by the responsible analyst.
11.12	All reference substances prepared in the laboratory or supplied externally should be retested at regular intervals to ensure that deterioration has not occurred.
11.14	In the case that the result of retesting of a reference substance is noncompliant, a retrospective check of tests performed using this reference substance since its previous examination should be carried out. For evaluation of outcomes of retrospective checks and consideration of possible corrective actions, risk analysis should be applied.

11.15	Pharmacopoeial reference substances are regularly retested and the validity (current status) of these reference substances is available from the issuing pharmacopoeia by various means, e.g. web sites or catalogues. Retesting by the laboratory is not necessary, provided the reference substances are stored in accordance with the storage conditions indicated

12. Calibration, verification of performance and qualification of equipment, instruments and other devices	
Clause	**Requirement**
12.1	Each item of equipment should be uniquely identified.
12.2	Each item of equipment should be labeled to indicate the status of qualification and the date when re-qualification is next required.
12.3	When installed, the equipment should be subjected to supplier IQ/OQ.
12.4 -12.5	There must be a detailed plan for the qualification of all equipment and instrumentation
12.6	Specific procedures should be established for each type of measuring equipment, taking into account the type of equipment, the extent of use and supplier's recommendations .e.g. pH and balances
12.7	Equipment should be operated only by authorized personnel and instrument manuals and SOPs on the use, maintenance, verification, calibration, qualification should be available
12.8	Maintenance and qualification records should be available for each of the instruments.
12.9	Each instrument shall have a usage/maintenance logbook.
12.10	Instrument maintenance procedures should be established.
12.11	"out of service" equipment should be appropriately marked.
12.12	Following service, qualification or maintenance, instrumentation should be appropriately authorized and signed back into use.

13. Traceability	
Clause	**Requirement**
13.1	The results of all analyses should be traceable, where appropriate, ultimately to a primary reference substance.
13.2	The calibration or qualification of instrument procedures should be traceable to a certified reference material and to SI units (metrological traceability).

14. Incoming samples	
Clause	**Requirement**
14.1-14.3	The laboratory shall collaborate with the sample provider to ensure that it obtains sufficient information about samples and objectives of testing and that the required analysis is performed and reported.
14.4	The laboratory should have a sampling plan and an internal procedure for sampling available to all analysts and technicians working in the laboratory.

	There should be an SOP for sampling and staff members who perform sampling should be appropriately trained and provided with appropriate equipment.
14.5-14.6	A standard test request form should be filled out and should accompany each sample submitted to the laboratory provided with the appropriate information.
14.7-14.11	The laboratory shall document the review of the request form and document the visual inspection of the sample on receipt.
14.8-14.10	the laboratory shall register the sample with an assigned unique registration number and the sample shall be legibly labeled
14.12	Samples should be appropriately stored and storage areas should be monitored for the environment.
14.13	The specific unit to which the sample is sent for testing is determined by the person responsible.
١٤.١٤	The examination of a sample should not be started before the relevant test request has been received.
١٤.١٥	The sample should be properly stored until all relevant documentation has been received.
١٤.١٦	A request for analysis may be accepted verbally only in emergencies. All details should immediately be placed on record pending the receipt of written confirmation.
١٤.١٧	Unless a computerized system is used, copies or duplicates of all documentation should accompany each numbered sample when sent to the specific unit.

15. Analytical Worksheets and Laboratory Notebooks

Clause	Requirement
15.1	The information about the sample, test procedure, calculations and the results of testing should be recorded in worksheets or notebooks and should be complemented by the raw data obtained in the analysis.
15.2	The record should provide sufficient information to confirm that the sample was tested in accordance with the requirements or support an OOS result.
15.3	There should be a separate record for each sample.
15.5	The record should provide the following information: (a) the registration number of the sample; (b) page numbering; (c) the date of the test request; (d) the date on which the analysis was started and completed; (e) the name and signature of the analyst; (f) a description of the sample received; (g) references to the specifications and a description of test method; (h) the identification of the test equipment used; (i) the identification number of any reference substance and the lot No's of the reagents used; (j) if applicable, the results of the system suitability test; (k) the identification of reagents and solvents used;

	(l) the results obtained; (m) the interpretation of the results and the final conclusions;
15.6	The record should be completed contemporaneously.
15.7	All the results obtained should be appropriately checked by a second analyst and signed and appropriately signed, approved and authorized
15.8	Errors should be appropriately corrected
15.10	current versions of the relevant pharmacopoeias should be used in the laboratory
15.11	Analytical records should be appropriately archived.

16. Validation of analytical procedures

Clause	Requirement
16.1	The laboratory should perform appropriate validation or verification procedures for the analytical methods employed for testing.
16.2	The laboratory should have a written process describing all elements of method validation
16.3	The SOP should describe which analytical performance characteristics need to be verified for the various types of analytical procedures which are routinely undertaken and the different verification/validation requirements for pharmacopoeia methods, manufacturers' methods and methods developed by the laboratory?
16.4	The laboratory should perform system suitability testing, where appropriate.
16.5	A major change to the analytical procedure, or in the composition of the product tested, or in the synthesis of the API, will require revalidation of the analytical procedure.

17. Testing and Reporting

Clause	Requirement
17.1	Samples should be tested according to an approved or authorized plan where any deviations should be adequately recorded During analysis samples should be stored securely
17.2	All deviations from the provided method should be adequately documented and explained.

18. Evaluation of test results Reports and Certificates of Analysis

Clause	Requirement
18.1	An SOP is required to describe the review and evaluation of test results and describe: (a) Where statistics should be employed, (b) The confirmation of compliance with the specification (c) How doubtful or atypical results are investigated, and definition of decision rules. (d) The investigation of OOS. (e) Trend analysis
18.2-18.5	An SOP is required for describing the investigation when a doubtful result (suspected OOS result) has been identified
18.6	The final analytical test report should compile the results and provide a conclusion of the examination of a sample and based on the analytical worksheet.

18.7	If a report requires any amendments a new corrected document should be issued.
18.11	The analytical report should provide the following content: (a) The laboratory registration number of the sample. (b) The laboratory test report number. (c) The laboratory testing the sample. (d) The originator of the request for analysis. (e) Full details of the sample. (f) The purpose of the investigation. (g) A reference to the specifications employed or the test methods used. (h) The results of all the tests obtained. (i) A discussion of the results obtained. (j) A conclusion as to whether or not the sample complied with the specification. (k) The date on which the test(s) was (were) completed. (l) The signature of the head of the laboratory or authorized person. (m) The name and address of the original manufacturer and, if applicable, those of the re-packer and/or trader. (n) The date on which the sample was received. (o) The expiry date or retest date.

19. Certificates of analysis

Clause	Requirement
19.1	The COA should contain the following information: (a) The registration number of the sample. (b) Date of receipt. (c) The name and address of the laboratory testing the sample. (d) The name and address of the originator of the request for analysis. (e) The name, description and batch number of the sample. (f) The name and address of the original manufacturer. (g) The reference to the specification used for testing the sample. (h) The results of all tests performed. (i) a conclusion as to whether or not the sample was found to be within the limits of the specification; (j) Expiry date or retest date if applicable. (k) Date on which the tests were completed. (l) The signature of the hea (m) (n) d of laboratory or another authorized person.

20. General Safety Rules	
Clause	**Requirement**
20.1	ALL staff members should be provided with appropriate, documented safety training.
20.2	The laboratory should have procedures and enforce "Good Practice" regarding the following: (a) Use of safety data sheets (MSDS). (b) Smoking, eating and drinking in the laboratory. (c) Use of fire-fighting equipment. (d) Wearing protective clothing and eye protection. (e) Use and handling highly potent, infectious or volatile substances. (f) Use and handling of highly toxic and/or genotoxic substances (see above). (g) Use of warning labels on all containers of chemicals. (h) Spark proofing of solvent stores. (i) Rules on safe handling of cylinders of compressed. (j) Rules regarding working alone. Instructing staff in first-aid techniques and emergency care and availability of first-aid materials, including safety showers and eye wash stations.
20.3	The laboratory should have rules regarding: (a)Mouth pipetting (b) Safe handling of glassware, corrosive reagents and solvents , (c)Warnings provided regarding exothermic reactions (d) Use of oxidizing or radioactive agents, (e)Disposal of chemicals. (f) Use of known carcinogens and mutagens as reagents.

Microbiology GLP check-list

Clause	Requirements
	1-General structural requirements
1.1	The laboratory should be a legal entity (licensed), or a defined part of a legal entity, that is legally responsible for its laboratory activities.
1.2	The laboratory should: define the organization and management structure of the laboratory, its place in any parent organization (organogram), and the relationships between management, technical operations and support services; Specify the responsibility, authority and interrelationship of all personnel who manage, perform or verify work affecting the results of laboratory activities; document its procedures to the extent necessary to ensure the consistent application of its laboratory activities and the validity of the results.
1.3	The laboratory should be committed to impartiality and confidentiality agreements to prevent any conflict of interest and should have to demonstrate how to eliminate any risks, if present, to both impartiality and confidentiality.
	2-Personnel
2.1	Current job descriptions for all personnel involved in any activity in the laboratory including tests and/ or calibrations, validations and verifications should be available (including technicians).
2.2	Microbiological testing should be either performed or supervised by an experienced person, qualified to degree level in microbiology or equivalent.
2.3	Staff should have basic training in microbiology and relevant practical experience before being allowed to perform work covered by the scope of testing (Training evidence or records should be documented).
2.4	If the laboratory includes opinions and interpretations of test results in reports, this shall be done by authorized personnel with suitable experience (Authorization evidence should be available).
2.5	Ongoing competence should be monitored objectively with provision for retraining where necessary.
2.6	Personnel should be trained in necessary procedures for the safe handling and containment of microorganisms within the laboratory facility
	3-Environment
	3.1-Premises
3.1.1	The microbiology laboratory should be separated from production area and restricted to authorized personnel only.
3.1.2	Microbiology laboratories should be designed to suit the operations to be carried out in them. There should be sufficient space for all activities to avoid mix ups, contamination

	and cross-contamination.
3.1.3	Laboratories should be appropriately designed (smooth surfaces) to enable appropriate cleaning, disinfection and minimize the risks of contamination.
3.1.4	There should be separate air supply with appropriate quality and free of contamination to laboratories and production areas.
3.1.5	Temperature and humidity controls and records should be in place for microbiological laboratories.
3.1.6	Personnel should be made aware of the appropriate entry and exit procedures including gowning.
3.1.7	Consideration should be given to designing appropriate classified areas for the operations to be performed within the microbiology laboratory based on the criticality of the product and the operation being carried out in the area.
3.1.8	Sterility testing should be performed under the same class as used for sterile/aseptic manufacturing operations and dedicated to testing sterile products only.
3.1.9	In general, laboratory equipment should not be routinely moved between areas of different cleanliness class or used outside the microbiology area, unless there are specific precautions in place to prevent cross-contamination.
	3.2-Environmental monitoring in the laboratory
3.2.1	(a) Where necessary and appropriate (e.g. in areas for sterility testing) an environmental monitoring program should be in place which covers, for example, use of active air monitoring, air settling or contact plates, temperature and pressure differentials. (b) Alert and action limits should be defined. (c) Trending of environmental monitoring results should be carried out.
	3.3-Cleaning, disinfection and hygiene
3.3.1	There should be a documented cleaning and disinfection program.
3.3.2	There should be a procedure for dealing with spillages.
3.3.3	Adequate hand-washing and hand-disinfection facilities should be available.
	3.4-Sterility test facilities
3.4.1	The sterility testing should be carried out within a Grade A unidirectional airflow protected zone or a biosafety cabinet (if warranted), which should be located within a clean room with a Grade B background. Alternatively, the testing can be carried out within a barrier isolator.
3.4.2	The clean-room classification and air-handling equipment of the sterility test facilities should be re-qualified at least annually by a competent person or contractor.
3.4.3	The environment should comply with the non-viable and viable limits, and verification of high efficiency particulate air (HEPA) filter integrity and room airflows should be performed.
3.4.4	Mapping locations for sample points for routine monitoring should be documented, as well as exposure duration, and frequency of all types of microbiological environmental

	monitoring should be specified in written procedures.
3.4.5	Air supplied to Grade A and B zones should be via terminal HEPA filters.
3.4.6	Appropriate airflow alarms and pressure differentials and indication instruments should be provided.
3.4.7	Room pressure readings should be taken and recorded from externally mounted gauges (labeled to indicate the area served and the acceptable specification) unless a validated continuous monitoring system is installed. As a minimum, readings should be taken prior to entry of the operator to the test suite.
3.4.8	Entry to the clean room should be via a system of airlocks and a change room where operators are required to put on suitable clean-room garments. The final change room should be under "at rest" conditions of the same grade as the room it serves.
3.4.9	(a) Garments for the sterility test operator should at minimum comply with the following: (b) -Outdoor clothing should not be brought into changing rooms leading to Grade B and C rooms. (c) For every worker in a Grade A/B area, clean sterile (sterilized or adequately sanitized) protective garments should be provided at each work session. (d) -Gloves should be regularly disinfected during operations. (e) Masks and gloves should be changed at least every working session. (f) -Operators working in Grade A and B areas should wear sanitized goggles. (g) -Wrist-watches, cosmetics and jewelry should not be worn in clean areas. (h) -Clothing used in clean areas should be laundered or cleaned in such a way that it does not gather additional particulate contaminants that can later be shed. Separate laundry facilities for such clothing are desirable. (i) -Washing and sterilization operations should follow standard operating procedures. (j) Operators should be trained and certified in gowning procedures with training records maintained.
3.4.10	The fittings and finishes of the premises should comply with the following:
3.4.10.1	Grade A and B areas should be designed so that all operations can be observed from outside.
3.4.10.2	In clean areas all exposed surfaces should be smooth, impervious and unbroken to minimize the shedding or accumulation of particles or microorganisms and to permit the repeated application of cleaning agents and disinfectants, where used.
3.4.10.3	To reduce the accumulation of dust and to facilitate cleaning, there should be no uncleanable recesses and a minimum of projecting ledges, shelves, cupboards and equipment.
3.4.10.4	Swing doors should open to the high-pressure side and be provided with self-closers.
3.4.10.5	False ceilings should be sealed to prevent contamination from the void space above them.

3.4.10.6	(a) Changing rooms should be designed as airlocks and used to provide physical separation of the different stages of changing and so minimize microbial and particulate contamination of protective clothing. (b) They should be flushed effectively with filtered air. The final stage of the changing room should, in the at-rest state, be the same grade as the area into which it leads. (c) The use of separate changing rooms for entering and leaving clean areas is sometimes desirable (d) In general hand-washing facilities should be provided only in the first stage of the changing rooms. (e) There should not be a change of more than one grade between airlocks or passages and changing rooms, i.e. a Grade D passage can lead to a Grade C airlock, which leads to a Grade B changing room, which leads to a Grade B clean room. (f) Changing rooms should be of a sufficient size to allow for ease of changing. Changing rooms should be equipped with mirrors so that personnel can confirm the correct fit of garments before leaving the changing room.
3.4.10.7	Airlock doors should not be opened simultaneously. An interlocking system and a visual and/or audible warning system should be operated to prevent the opening of more than one door at a time.
3.4.10.8	(a) A filtered air supply should be used to maintain a positive pressure and an airflow relative to surrounding areas of a lower grade under all operational conditions; it should flush the area effectively. (b) Adjacent rooms of different grades should have a pressure differential of approximately ١٠–١٥Pascal (guidance value). Particular attention should be paid to the protection of the zone of greatest risk, i.e. the immediate environment to which the product and the cleaned components in contact with it are exposed. (c) -It should be demonstrated that airflow patterns do not present a contamination risk; for example, care should be taken to ensure that particles from an operation is not conveyed to a zone of higher product risk. (d) A warning system should be operated to indicate failure in the air supply. (e) Indicators of pressure differentials should be fitted between areas where this difference is important, and the pressure differentials should be regularly recorded and failure alarmed.
3.4.11	(a) Environmental microbiological monitoring should be done in every work session under dynamic conditions and should reflect the facility used (room or isolator) and include a combination of air and surface sampling methods appropriate to the facility. (b) There should be written specifications, including appropriate alert and action limits for microbial contamination.

4- Validation of test methods	
4.1	(a) Standard (pharmacopoeial) test methods are considered to be validated. (b) The laboratory should demonstrate that the performance criteria of the standard test method can be met by the laboratory before introducing the test for routine purposes (method verification) and that the specific test method for the specific product is suitable (test method suitability including positive and negative controls).
4.2	(a) Test methods not based on compendial or other recognized references should be validated before use. (b) The validation should comprise, where appropriate, determining accuracy, precision, specificity, limit of detection, limit of quantitation, linearity and robustness. (c) The validation results should be evaluated with appropriate statistical methods, e.g. as described in the national, regional or international pharmacopoeias.
5-Equipement	
Each item of equipment, instrument or other device used for testing, verification and calibration should be uniquely identified.	
5.1-Maintenance of equipment	
5.1.1	(a) Maintenance and cleaning of essential equipment should be carried out at predetermined intervals in accordance with a documented procedure. (b) Detailed records should be kept.
5.2-Qualification	
5.2.1	Equipment, instruments and other devices should be designed، constructed, adapted, located, calibrated, qualified, verified and maintained as required by the operations to be carried out in the local environment. The user should purchase the equipment from an agent capable of providing full technical support and maintenance when necessary.
5.2.2	The laboratory should have the required test equipment, instruments and other devices for the correct performance of the tests and/or calibrations, validations and verifications (including the preparation of samples and the processing and analysis of test and/or calibration data).
5.2.3	Equipment, instruments and other devices, including those used for sampling, should meet the laboratory's requirements and comply with the relevant standard specifications, as well as being verified, qualified and/or calibrated regularly
5.3-Calibration, performance verification and monitoring of use	
5.3.1	The frequency of calibration and performance verification will be determined by documented experience and will be based on need, type and previous performance of the equipment.
5.3.2-Temperature measurement devices	
5.3.2.1	Where temperature has a direct effect on the result of an analysis or is critical for the correct performance of equipment, temperature measuring devices should be of appropriate quality to achieve the accuracy required

(e.g. liquid-in-glass thermometers, thermocouples and platinum resistance thermometers (PRTs) used in incubators and autoclaves) and their calibration should be traceable to national or international standards for temperature.

5.3.3-Incubators, water-baths and ovens

5.3.3.1 (a) The stability of temperature, uniformity of temperature distribution and time required to achieve equilibrium conditions in incubators, water-baths, ovens and temperature-controlled rooms should be established initially and documented (Thermal distribution studies), in particular with respect to typical uses (for example, position, space between, and height of, stacks of Petri dishes).

(b) The constancy of the characteristics recorded during initial validation of the equipment should be checked and recorded after each significant repair or modification.

(c) The operating temperature of this type of equipment should be monitored and records retained.

5.3.4-Autoclaves

5.3.4.1 (a) Autoclaves should be capable of meeting specified time and temperature tolerances; monitoring pressure alone is not acceptable.

(b) Sensors used for controlling or monitoring operating cycles require calibration and

(c) the performance of timers should be verified.

(d) The effectiveness of autoclave operation during each cycle may be checked by the use of chemical or biological indicators for sterilization or decontamination purposes.

5.3.4.2 (a) Initial validation should include performance studies (spatial temperature distribution surveys) for each operating cycle and each load configuration used in practice.

(b) This process must be repeated after any significant repair or modification (e.g. change to loading arrangements or operating cycle) or where indicated by the results of quality control checks on media or risk assessment.

(c) Sufficient temperature sensors should be positioned within the load (e.g. in containers filled with liquid/medium) to enable location differences to be demonstrated.

5.3.4.3 (a) Clear operating instructions should be provided based on the heating profiles determined for typical uses during validation/revalidation.

(b) Records of autoclave operations, including temperature and time, maintained for every cycle.

(c) Monitoring of autoclave may be achieved by one of the following:

— Using a thermocouple and recorder to produce a chart or printout.

— Direct observation and recording of maximum temperature achieved and time at that temperature.

	5.3.5-Weights and balances
5.3.5.1	Weights and balances shall be calibrated traceably at regular intervals (according to their intended use) using appropriate standard weights traceable to certified standard weights.
	5.3.6-Volumetric equipment
5.3.6.1	Microbiology laboratories should carry out initial verification of volumetric equipment (automatic dispensers, dispenser/diluters, mechanical hand pipettes and disposable pipettes) and then make regular checks, as appropriate, to ensure that the equipment is performing within the required specification.
5.3.6.2	(a) For "single-use" disposable volumetric equipment, laboratories should obtain supplies from companies with a recognized and relevant quality system. (b) If the supplier does not have a recognized quality system, laboratories should check each batch of equipment for suitability.
	5.3.7-Other equipment
5.3.7.1	(a) Conductivity meters, oxygen meters, pH meters and other similar instruments should be verified regularly or before each use. (b) The buffers used for verification purposes should be stored in appropriate conditions and should be marked with an expiry date. (c) Where humidity is important to the outcome of the test, hygrometers should be calibrated, the calibration being traceable to national or international standards. (d) Timers, including the autoclave timer, should be verified using a calibrated timer or national time signal. (e) When centrifuges are used in test procedures, an assessment of the rotations per minute (RPM) should be made. Where it is critical, the centrifuge should be calibrated.
	6-Reagents and culture media
	6.1-Reagents
6.1.1	Laboratories should verify the suitability of each batch of reagents critical for the test, initially and during its shelf-life.
	6.2-Media
6.2.1	Media may be prepared in-house or purchased either partially or fully prepared. Vendors of purchased media should be approved and qualified. The qualified vendor may certify some of the quality parameters. Where the supplier of fully prepared media is qualified and provides growth promotion certification per batch of media and transportation conditions have been qualified, the user may rely on the manufacturer's certificate with periodic verification of his or her results.
6.2.2	(a) Media should be prepared in accordance with any manufacturer's instructions, taking into careful account specifications such as time and temperature for sterilization. (b) Growth promotion and, if appropriate, other suitable performance tests should be done on all media on every batch and on every shipment.

6.2.3	Microwave devices should not be used for the melting of media due to the inconsistent distribution of the heating process.
6.2.4	Batches of media should be identifiable and listed, their conformance with quality specifications documented (e.g. growth promotion and inhibitory properties).
6.2.5	(a) Raw materials (both commercial dehydrated formulations and individual constituents) and media should be stored under appropriate conditions recommended by the manufacturer, e.g. cool, dry and dark. (b) All containers, especially those for dehydrated media, should be sealed tightly. (c) Dehydrated media that are caked or cracked or show a color change should not be used.
6.2.6	The suitable performance of culture media, diluents and other suspension fluids should be checked, with regard to: a. Recovery of 50–200% (after inoculation of not more than 100 colony-forming units (CFU) should be demonstrated; b. inhibition or suppression of non-target organisms; c. biochemical (differential and diagnostic) properties; and d. Other appropriate properties (e.g. pH, volume and sterility).
6.2.7	Water of a suitable microbiological quality and which is free from bactericidal, inhibitory or interfering substances, should be used for preparation unless the test method specifies otherwise.
6.2.8	Shelf-life of prepared media under defined storage conditions shall be determined and verified with a study and documented.
	6.3-Labeling
6.3.1	(a) Laboratories should ensure that all reagents (including stock solutions), media, diluents and other suspending fluids are adequately labeled to indicate, as appropriate, identity, concentration, storage conditions, preparation date, validated expiry date and/or recommended storage periods. (b) The person responsible for preparation should be identifiable from records.
	6.4-Organism resuscitation
6.4.1	• Organism resuscitation is required where test methodologies may produce injured cells. For example, exposure to: injurious effects of processing, e.g. heat; antimicrobial agents; preservatives; extremes of osmotic pressure; and Extremes of pH. • Organism resuscitation may be achieved by:

	exposure to a liquid media like a simple salt solution at room temperature for 2 hours; exposure to a solid repair medium for 4–6 hours.
7- Reference materials and reference cultures	
7.1-International standards and pharmacopoeial reference substances	
7.1.1	Reference materials and certified reference materials provide essential traceability in measurements and are used, for example; -to demonstrate the accuracy of results, - to calibrate equipment, - to monitor laboratory performance, - to validate methods, and - to enable comparison of methods. If possible, reference materials should be used in appropriate matrices.
7.2-Reference cultures	
7.2.1	(a) Reference cultures are required for establishing acceptable performance of media (including test kits), for validating methods and for assessing/evaluating ongoing performance. (b) To demonstrate traceability, laboratories must use reference strains of microorganisms obtained directly from recognized national or international collections
7.2.2	(a) Reference strains may be sub-cultured once to provide reference stocks. (b) Purity and biochemical checks should be made in parallel as appropriate. (c) It is recommended to store reference stocks in aliquots either deep-frozen or lyophilized. If reference stocks have been thawed, they must (d) not be refrozen and reused.
7.2.3	(a) Working cultures for routine use should be primary subcultures from the reference stock. (b) Working stocks should not normally be sub-cultured, usually not more than five passages from the original reference strain.
8-Sampling and sample handling	
8.1	For general principles reference is made to *WHO Good practices for pharmaceutical quality control laboratories* (*1*).
8.2	In many cases, testing laboratories are not responsible for primary sampling to obtain test items. Where they are responsible, it is strongly recommended that this sampling be covered by a quality assurance system and regular audits.
8.3	(a) The laboratory should have procedures that cover the delivery of samples and sample identification. (b) It is important to check and record the condition of the sample on receipt by the laboratory. (c) The storage conditions should be monitored and records kept. (d) The responsibility for transport, storage between sampling and arrival at the testing laboratory should be clearly documented.

8.4	(a) Sampling should only be performed by trained personnel (documented training). (b) It should be carried out aseptically using sterile equipment, appropriate precautions should be taken to ensure that sample integrity is maintained through the use of sterile sealed containers for the collection of samples where appropriate. (c) It may be necessary to monitor environmental conditions, for example, air contamination and temperature, at the sampling site or booth. (d) Time of sampling should be recorded, if appropriate.
8.5	(a) Sub-sampling by the laboratory immediately prior to testing may be required as part of the test method. It may be appropriate that it is performed according to national or international standards, where they exist, or by validated in-house methods. (b) Sub-sampling procedures should be designed to collect a representative sample.
8.6	A procedure for the retention and disposal of samples shall be written. Samples should be stored (retained) until the test results are obtained, or longer if required
9-Disposal of contaminated waste material	
9.1	(a) The procedures for the disposal of contaminated materials should be designed to minimize the possibility of contaminating the test environment or materials. (b) It is a matter of good laboratory management and should conform to national/international environmental or health and safety regulations.
10-Quality assurance of results/quality control of performance	
10.1	Internal quality control consists of all the procedures undertaken by a laboratory for the continuous evaluation of its work. The main objective is to ensure the consistency of results day to day and their conformity with defined criteria.
10.2	A program of internal periodic checks is necessary to demonstrate that variability (i.e. between analysts and between equipment or materials etc.) is under control. All tests included in the laboratory's scope of accreditation need to be covered. The program may involve: (a) the use of spiked samples (b) the use of reference materials (including proficiency testing scheme materials) (c) replicate testing (d) replicate evaluation of test results The interval between these checks will be influenced by the construction of the program and by the number of actual tests. It is recommended that, where possible, tests should incorporate controls to monitor performance.
10.3	External quality assessment (proficiency testing): Laboratories should regularly participate in proficiency testing which are relevant to their scope of accreditation; preference should be given to proficiency testing schemes which use appropriate matrices. Laboratories should use external quality assessment not only to assess laboratory bias but also to check the validity of the whole quality system.

11-Testing procedures	
11.1	Testing should normally be performed according to procedures described in the national, regional and international pharmacopoeias.
11.2	Alternative testing procedures may be used if they are appropriately validated and equivalence to official methods has been demonstrated.
12-Test reports	
12.1	(a) If the result of the enumeration is negative, it should be reported as “not detected for a defined unit” or “less than the detection limit for a defined unit”. The result should not be given as “zero for a defined unit” unless it is a regulatory requirement. (b) Qualitative test results should be reported as “detected/not detected in a defined quantity or volume”.
12.2	Where an estimate of the uncertainty of the test result is expressed on the test report, any limitations (particularly if the estimate does not include the component contributed by the distribution of microorganisms within the sample) have to be made clear to the client.