MEDICINES CONTROL COUNCIL

DEPARTMENT OF HEALTH
Republic of South Africa

MEDICINES CONTROL COUNCIL

SCREENING TEMPLATE FOR NEW APPLICATIONS FOR REGISTRATION

The Screening Template is to be used on receipt of an application for registration of a medicinal product for human or veterinary use submitted to the South African Regulatory Authority.

Usually a separate application for each pharmaceutical form is required.

MRF1*		CTD		~~eCTD~~	

In the case of a Complementary Medicine, only sections A.1 and A.2 are currently applicable.

A ADMINISTRATIVE

A.1 SCREENING – PAPER SUBMISSIONS

Product and dossier information(C = Critical)			
1	Applicant	**C**	*<LICENSED NAME>*
2	Product reference number		
3	Product proprietary name	**C**	*<Name, strength; pharmaceutical form>*
4	Dosage form		*<pharmaceutical form>*
5	†API/s		*<APIs>*
6	Complementary discipline(s)	**C**	
7	Screening fee included (cheque or proof of payment, submitted in a separate envelope, with copy of the covering letter)	**C**	Y ☐ N☐
8	Date of covering letter/letter of application		
9	Date of receipt		*<date submitted>*

*Veterinary applications

† Refer to guideline on Quality, Safety and Efficacy of Complementary Medicines

Product and dossier information(C = Critical)					
10	Box size (A4 box)	**C**	Y ☐	N ☐	
11	Number of boxes				
12	Are the boxes clearly labelled on the side to specify the number and content of each box, e.g. Modules/Parts, sample, covering letter (MRF1)/letter of application (Module 1.0), cheque or proof of payment and product identification code/ product name?		Y ☐	N ☐	
13	Does a red sticker indicate the screening phase?		Y ☐	N ☐	
14	Is the dossier correctly bound? (No lever arch files, ring binders, or metal binders;maximum4 cm thick including binder, but not over-full for the binder used)	**C**	Y ☐	N ☐	
15	Have dividers been included in the paper submission?	**C**	Y ☐	N ☐	
16	Are all the modules/PARTs copied double-sided except for the PI and PIL (Module 1.3)?	**C**	Y ☐	N ☐	
17	Is a sample included in an envelope? (screening phase)	**C**	Y ☐	N ☐	
18	Is a sample provided for the smallest pack size?		Y ☐	N ☐	
19	Is the approval letter for “fast track” status included if relevant?		Y ☐	N ☐	N/A ☐
20	Module 1.2.1(c) / PART 1A				
20a	Is it signed by the authorised pharmacist (original signature)? *(pp not accepted; scanned signature not accepted; consultant may not sign)*	**C**	Y ☐	N ☐	
20b	Has the designation of the pharmacist been indicated?		Y ☐	N ☐	
20c	Has the application been dated?	**C**	Y ☐	N ☐	
21	Are Modules / PARTs 1-5 included?	**C**	Y ☐	N ☐	
22	Different strengths		Y ☐	N ☐	
21a	Are different strengths submitted in one application *(check presentation & dosage)?*		Y ☐	N ☐	N/A ☐
21b	Does the letter of application clearly indicate different strengths?	**C**	Y ☐	N ☐	N/A ☐
21c	Has a separate Module 1.2.1 been submitted for each strength?	**C**	Y ☐	N ☐	N/A ☐
22	Are the documents, including copies of chromatograms and chromatogram text in Modules 5.3.1 & 3.2.S / PARTs 2A & 3A, legible?	**C**	Y ☐	N ☐	

Type of application: Indicate the type of medicine, the submission type and data included as proof of efficacy, and the review procedure using a check mark (✓) or a cross (X) (as in Module 1.2.1):
(Note: Include only the relevant table for either orthodox or complementary medicine)

Orthodox medicine

Human Medicine:		***Submission type:***		***Data as proof of efficacy:***	
Pharmaceutical		*NCE*		*~~Pre~~Non-clinical*	
Biological		*Multisource*		*Clinical*	
Veterinary Medicine:		*Biosimilar*		*Biostudy*	
Pharmaceutical		*Line Extension*		*Other*	
Biological		*Call-up*			
Review Procedure:					
Routine		*AMRP*		*Expedited (Fast Track)*	

Complementary Medicine

Complementary Human Medicine:		***Data as proof of efficacy:***			
First application		*Low risk claim*		*Literature*[1]	
Line Extension				*Clinical*	
				~~Pre~~Non-clinical	
Complementary Veterinary Medicine:		*High risk claim*		*Literature*	
First application				*Clinical*[2]	
Line Extension				*Non-clinical*	
				Biostudy	
				Biowaiver/dissolution	
Review Procedure:					
Routine		*Expedited (Fast Track)*			

[1] *Required for low risk claim*
[2] *Required for high risk claim*

NOTES:

1. *The questions marked **C** are regarded as critical for acceptance of the application.*
2. *Return the application to the applicant if any critical issues are non-compliant.*

A.2 POST-SCREENING FOR PAPER SUBMISSIONS

Product and dossier information (C = Critical)			
1	Applicant	**C**	*<LICENSED NAME>*
2	Product reference number		
3	Product proprietary name	**C**	*<Name, strength; pharmaceutical form>*
4	Dosage form		*<pharmaceutical form>*
5	‡API/s		*<APIs>*
6	Complementary discipline(s)	**C**	
7	Application fee included (cheque or proof of payment, submitted in a separate envelope, with copy of the covering letter)	**C**	Y ☐ N ☐
8	Date of covering letter/letter of application ‡		
9	Date of receipt		*<date submitted>*
10	Box size (A4 box)	**C**	Y ☐ N ☐
11	Number of boxes		*<No.>*
12	Are the boxes clearly labelled on the side to specify the number and content of each box, e.g. set numbers, Modules/Parts, covering letter (MRF1)/letter of application (CTD 1.0), cheque or proof of payment and product identification code/ product name?	**C**	Y ☐ N ☐
13	Does a green sticker indicate the post-screening phase?		Y ☐ N ☐
14	Is the dossier correctly bound? (No lever arch files, ring binders, or metal binders; maximum 4 cm thick including binder, but not over-full for the binder used)	**C**	Y ☐ N ☐
15	Have labelled tabbed dividers been included, not only to indicate the location of the Modules, but also subsections?	**C**	Y ☐ N ☐
16	Are all the modules/PARTs copied double-sided except for the PI and PIL?	**C**	Y ☐ N ☐
17	Is Module 1.2.1(c) / PART 1A signed by the authorised pharmacist (original signature), & dated? *(pp or scanned signature not accepted; consultant may not sign)*	**C**	Y ☐ N ☐
18	Are the documents, including copies of chromatograms and chromatogram text in Modules 5.3.1 & 3.2.S / PARTs 2A & 3A, legible?	**C**	Y ☐ N ☐

NOTES:

1. *The questions marked **C** are regarded as critical for acceptance of the application.*
2. *Return the application to the applicant if any critical issues are non-compliant.*

‡ Refer to guideline on Quality, Safety and Efficacy of Complementary Medicines

B TECHNICAL VERIFICATION - PHARMACEUTICAL QUALITY ASSESSOR

Applicant to indicate location in dossier in the "Yes" Column

Critical Pharmaceutical Quality Information		Yes (Y)	No (N)
1	Stability data on the active pharmaceutical ingredient (API):		
1a	NCE: At least 12 months long-term and 6 months accelerated?[§]		
1b	Well-known: At least 6 months long-term and 3 months accelerated OR supporting literature[§]		
2	Module 3.2.S/ PART 3A		
2a	Is Module 3.2.S/ PART 3A for each manufacturer of API included?		
2b	If a biostudy is submitted, is Module 3.2.S/PART 3A included for the API manufacturer of the biostudy test product, even if this API manufacturer is not being applied for? (*cf*1.2.2.3 for CTD)		
2c	Confirm that the API is not a mixture with another API or IPIs		
2d	Where more than one manufacturer of the API (not the same parent company) is used, are comparative chemical and physical data in tabular format included to demonstrate equivalence?		
2e	Has the comparative chemical and physical data been generated by the same testing laboratory (laboratory stated) under the same conditions?		
2f	Where more than one site of the same parent company is used and an identical method of synthesis is used at these sites has a statement to this effect been included?		
2g	Have valid CoAs of the API issued by each site for at least two batches been included?		
2h	If a CEP is submitted, is the declaration of access completed?		
3	Stability data on the pharmaceutical product (FPP):		
3a	NCE: At least 12 months long-term and 6 months accelerated?		
3b	Generics: At least 9 months long-term and 3 months accelerated?		
3c	Is a tabulated summary of the batches, i.e. sizes, numbers, type, packaging material, and conditions and period of testing included for each manufacturer?		
3d	Are details of the API manufacturer, container, batch number, batch size, date of manufacture of the batch, and storage conditions reflected in Module 3.2.P.8.1 or Module 3.2.P.8.3/ PART 3G?		
3e	Have stability data been derived with API sourced from the manufacturer identified in Module 3.2.S.2.1/ PART 3A(b)?		
3f	Is the API manufacturer identified in Module 3.2.S.2.1(refer Module 1.2.2.3) / PART 3A(b) the same as that of -		
	a) the biostudy test batch?		
	b) developmental batches?		

[§]Storage conditions as defined in current official Stability Guideline

Critical Pharmaceutical Quality Information		Yes (Y)	No (N)
3g	If the answer is NO to any question in 3f, are pharmaceutical equivalence data of the API manufacturers included in Module 3.2.R.4 / PART 3A(c)?		
3h	Have stability data been derived from the product packed in packaging material(s) detailed in Module 3.2.P.7 / PART 3D?		
3i	Are validation data for the stability testing assay method (if not pharmacopoeial and/or different to that in Module 3.2.P.5.2/PART 3F) included?		
3j	Are validation data included for the method(s) used to test degradation products?		

C TECHNICAL VERIFICATION - BIOEQUIVALENCE DATA

Applicant to indicate location in dossier in the "Yes" Column

Critical Information		Yes (Y)	No (N)
1	Is/are the fasting and/or fed bioequivalence study(ies) in compliance with the Biostudies guideline requirements for the design and conduct of studies for immediate or modified release products, as applicable?		
2	Are the following components of the biostudy included:		
2a	Date and place of study?		
2b	The protocol?		
2c	Evidence of ethical approval?		
2d	Analytical report - All individual subject concentration data?		
2e	Assay validation plus representative chromatograms from analytical runs for 20 % of all subjects (or for a minimum of 4 subjects whichever is the greater, to a maximum of 8 subjects) including chromatograms for the associated standards and quality control samples, and do they comply with the requirements for legibility?		
2f	Individual concentration data and pharmacokinetic parameters listed by formulation with summary statistics such as geometric mean, median, arithmetic mean standard deviation, coefficient of variation, minimum and maximum?		
2g	All individual plasma concentration vs. time profiles presented on a linear/linear as well as log/linear scale?		
2h	CoAs and dissolution profiles of test and reference products and CoA of API of test product.		
2i	Investigator's *curriculum vitae*?		
2j	Quality assurance statement?		
3	Have all the individual patient Case Report Forms (CRFs) and individual patient line listings been removed?		
4	Batch size of the test product		
4a	Is the batch size a minimum of 100 000 units or at least 10 % of the production batch, whichever is greater?		
4b	If the batch size is less than 100 000 units, has the use of a smaller batch size been motivated/justified?**		
5	Has the country of procurement of the reference product and name and address of the relevant applicant been stated?		
6	Was the reference product procured in a country with which the MCC aligns itself?		
7	Is the biostudy reference product strength within the MCC approved package insert dose range?		
8	If relevant, has a full report on comparative data to demonstrate equivalence of the foreign reference product to the S.A. registered innovator product submitted?		

** If the production batch size is smaller than 100 000 units, a full production batch should be used.

Critical Information		Yes (Y)	No (N)
9	If the biostudy test product **was not** manufactured by the same manufacturer, at the same site, with API(s) manufactured by the same API manufacturer being applied for:		
9a	Has pharmaceutical equivalence of the API manufacturer of the biostudy and developmental batches been established with the API manufacturer being applied for? (DMFs, comparative analysis from same laboratory, discussion of routes of synthesis, FP stability data and comparative dissolution to confirm similarity of FP manufactured with API from the relevant sources, including full report in accordance with Dissolution guideline in the three dissolution media, pH's 1,2; 4,5 & 6,8)		
9b	Have appropriate quantitative methods, e.g. dissolution data in three media in accordance with the Dissolution guideline and Post-registration amendment guidelines, been used to confirm similarity of the FP manufactured by relevant manufacturers and manufacturing sites and		
9c	is a full report in accordance with the report format described in the Dissolution Guideline with the appropriate data included with this application [e.g. similarity (f2) factor]?		
10	If a biowaiver is requested for additional strengths of the product:		
10a	Are the additional strengths proportionally formulated?		
10b	Were the additional strengths manufactured by the same manufacturer, at the same site, with API(s) sourced from the same manufacturer?		
10c	Have appropriate quantitative methods, e.g. dissolution data in three media in accordance with the Dissolution guideline, been used to confirm similarity and		
	is a full report in accordance with the report format described in the Dissolution Guideline with the appropriate data included with this application [e.g. similarity (f2) factor]?		
11	If a BCS biowaiver is requested, are the following included:		
11a	a motivation and justification?		
11b	a full report in accordance with the report format described in the Dissolution Guideline with the appropriate data comparing the test and reference products in the three dissolution media, **pH's 1,2; 4,5** and **6,8?**		

D TECHNICAL VERIFICATION - PRE-CLINICAL AND CLINICAL INFORMATION

Applicant to indicate location in dossier in the "Yes" Column

Critical Information		Yes (Y)	No (N)
1	Are the proposed package insert (PI) and the proposed patient information leaflet (PIL) included in Module 1.3.1 / PART 1C?		
2	Is the information in the proposed PI cross-referenced to the locally submitted supporting evidence?		
3	Has the information in the proposed PIL been cross-referenced to the proposed PI?		
4	Has the information in Modules 2.4, 2.5, 2.6 and 2.7 been included? (or MRF1 PARTs 2D and 2E)		
5	Has the information of Modules 4 and 5 of the ZA CTD (MRF1 PARTs 4 & 5) been included and is the proposed PI cross-referenced to this information?		
6	Are the references referred to in the proposed PI included?		
7	Are the cross-references complete, accurate and properly indexed?		
8	Is the information in the proposed PI cross-referenced to acceptable references? *Note: SPI, Unregistered Old Medicines, MIMS and Micromedex are not acceptable references.*		
9	Is the information in the proposed PI based on the latest editions of the standard acceptable references?		
10	Are all references legible and of good quality?		
11	Have all the raw data (individual patient data and line listings) been removed?		

NOTES:

1. *In case of any one or more answers being "No", refer to MCC section coordinator.*
2. *Unless otherwise decided, the assessment should not commence if these matters have not been (adequately) addressed. The final decision could be made at the P&A and/or CCC meeting.*

UPDATE HISTORY

Date	Reason for update	Version & publication
June 2010	First publication released for implementation and comment	Version 3, June 2010
March 2011	Deletion of "strength" re separate applications	Version 4,March 2011
	Inclusion in sections B,C, D of applicant's use of form	
	Amendment of sections	
	A.1 5/9 & A.2 5/9 (letter of application); A.1 11 & A.2 11 (binding) A.1 14 (sample); A.1.16 & A.2 12 (signature) A.1 new 18 (different strengths)	
	Section B new 2b (API for Biostudy) and renumbered new 2c (API in mixture), 2e now 2g (CoAs) new 2h (CEP), B new 3f (API manufacturer) new 2h (CEP) 3d & 3g (API source changed to manufacturer) new 3f (API manufacturer) and renumbered	
	Section C 2d (Chromatograms maximum of 8 subjects) new 4 (Batch size of the test product) new 9 (Biostudy test product requirements) new 10a (under biowaivers) and renumbered	
	D 4 & 5 (reference to MRF1)	
1 April 2011	Implementation	Version 4,March 2011
March 2011	A.1 & A.2 new pt 4 included, names of APIs	Version 4_1, March 2011
1 May 2011	Implementation	
May 2011	Amendment of Section A.1 – new 20 Amendment of Section C 2 – new 2d, 2f, 2g, 2h; renumbered	Version 5, June 2011
With immediate effect	Implementation	
March 2012	Amendment of Section A.1 – new 14 and Section A.2 – new 13 and renumbered accordingly	Version 5_1, June 2011
With immediate effect	Implementation	
March 2013	Amendment of Section A.1 – reference to paper submissions in the heading, new 4, renumbered, inclusion of section on type of application Amendment of Section A.2 – new 4, renumbered	Version 6, March 2013
	Inclusion of new Section A.3 for eCTD	
	Amendment of Section D - Inclusion of new 8, 9, 10	
With immediate effect	Implementation	
April 2014	Amended to include Complementary Medicines Section A.1 - new 6, 20a amended, new 20b & c, renumbered, new Type of Applications Section A.2 - new 6, new 15, 17 amended, renumbered A.3.1 Submission type included. Correction B 3g	Version 7, April 2014
With immediate effect	Implementation	
June 2014	Removal of eCTD to separate template Amendment to Type of Application, Orthodox (non-clinical) Amendment to Type of Application, Complementary, Data	Version 8, Aug 2014
With immediate effect	Implementation	