South African Health Products
Regulatory Authority
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OVER-ARCHING: GOOD REVIEW PRACTICE GUIDE

This guide is intended to provide guidance to applicants on Good Review Practices. It represents the South African Health Products Regulatory Authority's current thinking on the safety, quality and efficacy of medicines and the safety, quality and performance of medical devices. It is not intended as an exclusive approach. Good review practices (GRevPs) are considered as ways to improve the Authority performance and ensure the quality of the regulatory system. The goal of GRevPs is to promote the timeliness, predictability, consistency, transparency, clarity, efficiency, and high quality of the content and management of reviews and review reports for pharmaceuticals.

Document History

Final Version	Reason for Amendment	Effective Date
1	New Guide	22 June 2022
2		

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1 INTRODUCTION

The South African Health Products Regulatory Authority (SAHPRA) is striving and exerting efforts to become a strong and resilient regulatory authority so as to safeguard the health of the South African population from health risks associated with medical products marketed in the country.

Bearing in mind that the complex and multidisciplinary assessment approach of medical products; the authority endeavours to meet scientific and evidentiary standards for safety, efficacy and quality reviews. SAHPRA seeks the highest levels of quality in submitted applications, authority reviews and processes, and final regulatory decisions. Good review practices (GRevPs) are considered as ways to improve the Authority performance and ensure the quality of the regulatory system. The goal of GRevPs is to promote the timeliness, predictability, consistency, transparency, clarity, efficiency, and high quality of the content and management of reviews and review reports for pharmaceuticals. This is done through applying the fundamental values of accountability, communication, and consistency through the development of review tools (e.g. standard operating procedures, templates, and training) and the provision of scientific and regulatory information in print, in person, and online.

To promote continuous improvement, all aspects of Good Review Practices shall be evaluated and updated on an ongoing basis.

2 PURPOSE

The objective of this guideline is to provide high-level guidance on good review (GRevPs) principles and processes related with medical products dossier review. It is not intended to provide detailed instruction on how to conduct a scientific review.

3 SCOPE

This Guideline will be applicable to the review practices of safety, effectiveness and quality data of medical products.

4 RELATED DOCUMENTS

APPLICABLE STANDARDS, GUIDELINES, LEGISLATIONS AND REGULATIONS	
Title	Document Number
Med	N/A
General Information Guideline	2.01
Quality & Bioequivalence Guideline	2.02
Clinical Guideline	2.09
Guideline for patient information leaflet for human medicines (categories A and D)	2.14
Proprietary Names Guidelines	2.15
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Scheduling of Medicines Guidelines	2.36
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Summary of Critical Regulatory Elements (SCoRE)	6.31
Abridged review template	6.33
Verified review template	6.34

5 ABBREVIATIONS AND DEFINITIONS

Abbreviation / Term	Meaning
BAU	Business as usual
CEM	Clinical Evaluation Management
GRevPs	Good Review Practices
HPA	Health Products Authorisation
QMS	Quality Management System

Abbreviation / Term	Meaning
RRA	Recognized Regulatory Authority
SAHPRA	South African Health Products Regulatory Authority
SOP	Standard Operating Procedure

6 ACCOUNTABILITY

SAHPRA is accountable to the public for helping to ensure the safety, efficacy, and quality of medicinal products marketed in this country. SAHPRA is also accountable for a high-quality and efficient review process that produces timely and informed decisions. In addition, review staff are responsible for implementing GRevPs and associated policies and processes. Applicants are accountable for the quality and completeness of their applications, including optimal use of product development resources. The quality of submitted applications is vital to achieving timely and science-based regulatory decisions.

7 CLARITY

Communication that is clear, complete, and concise is key to ensuring transparency and clarity during application review. Transparency ensures that all stakeholders understand SAHPRA policies. Transparency also ensures that applicants are informed of review progress and allows for both applicants and review staff to anticipate and respond to potential issues and plan for next steps. Clarity allows SAHPRA assessment of the benefits and risks of a product as described in the application. Clarity also allows the applicant to understand the reasoning behind a given regulatory action. Communication necessary to achieve transparency during an ongoing review is expected to contain the highest possible degree of clarity.

8 CONSISTENCY

Consistent application and support of GRevPs by review staff and applicants are critical to the overall success of the marketing application review process. SAHPRA staff can exercise flexibility within the process when a thorough assessment of an individual situation justifies doing so. Process changes that become generally accepted as new best practices will be documented and shared for broader implementation.

9 QUALITY MANAGEMENT

All review processes shall be done in line with the quality management system (QMS) of the Authority. Dossier assessment shall be done in accordance with laid down procedures to ensure well-written and thorough report of assessment findings and conclusions. As part of the quality manual and quality management principles of the authority, the following main activities have been/has to be implemented to improve the GRevP of applications submitted to the authority.

- Develop and implement appropriate legal frameworks and detailed technical guidelines aligned with international practices.
- Develop and implement detailed, numbered and version controlled Standard Operating Procedure (SOPs) to guide the assessment process. These SOPs will be updated regularly as new and improved work practices are identified.
- Only standardized and approved assessment templates and checklists shall be used. The registration Units shall develop, maintain and implement numbered, version controlled and approved review templates and checklists for all review processes.

- There shall be timelines for reviewing applications for each category of application
- Define processes that clearly indicate decision-making processes which create transparency and accountability, such as decision frameworks, time frames for completion and communication modalities of reviews, use of external experts, public meetings and peer-reviews.
- Adhere and implement review processes defined and adhere to specified time frames.
- Offer professional development, mentoring and regular on-the-job training.
- Record and collect key documents, such as minutes of meetings and teleconferences, letters and reports.
- Ensure that review procedures and templates are being consistently interpreted and applied through the assessment of various inputs, such as internal and external feedback and periodic evaluation of practices by internal and external experts.
- Review documentation and decision-making processes regularly.
- Consider introducing improvements to the review and decision-making process. Conduct internal assessment of a review; peer-review; internal quality audits; self -assessments; analyses of feedback from stakeholders; post-approval analysis of the decision in collaboration with other authorities; the public and applicants; and analysis of impact on public health.

10 REVIEW PROCESS STAGES AND PATHWAYS

SAHPRA sets key stages in the process of reviewing medical products. Those include application submission, screening and evaluation. SAHPRA will make applicants aware on its expectations at all stages including the target time frames, guidelines, requirements, templates and checklists. All applications shall undergo screening and shall be done at the point of submission of applications. All the review process stages shall be done according to agreed laws, guidelines, checklists and templates provided for each category of applications. Review pathways are as follows:

Full review shall be conducted for new applications that are not approved by a Recognised Regulatory Authority (RRA). However, applications for medical products that are approved by an RRA (that meet SAHPRA requirements for reliance-based review) will follow the partial review process.

SAHPRA will make provision for priority review for the assessment and/or registration of medicines that treat serious diseases and are of major public interest.

11 REVIEW PERSONNEL

The Authority shall use a pool of experts or review advisory panel composed of internal staff and external experts. The experts and anyone who participates in the review process of dossiers shall be trained in certain sections of the dossier (dependent on job description) including administrative requirements; technical aspects of the medical product dossier- quality, safety, efficacy; and product information and labelling sections of the dossier including the national laws and guidelines.

General competencies required to conduct review work include:

Knowledge of statutes, regulations, guidelines and precedents, including international guidelines and precedents approved by SAHPRA

- Knowledge of the process of medical product development from early development phases to post-marketing surveillance and risk management;
- Scientific communication skills for written evaluations, public presentations and negotiation and consensus building with applicants and stakeholders

SAHPRA shall ensure the expertise and competencies of the experts involved in the review of medical products dossiers. Reviewers shall be assigned and engaged in the review process based on their specialization and expertise. Beyond their professional qualifications, reviewers should have the ability to critically appraise the information presented in an application and not just accept it as presented.

Considering the experience and expertise of the assessors, a dossier shall be reviewed by both primary and secondary assessors. The experts who took basic dossier assessment training shall participate as a primary assessor and shall be mentored by the secondary assessors. Secondary assessors who are more experienced shall review the dossier reviewed by primary assessor.

12 ASSESSMENTS REPORTS

The goal of an assessment report is that forms the basis for its regulatory decision. Documentation should not summarize the work that occurred over the course of a review, nor should it reiterate content that is found in the submission. Documentation should describe important issues that led to the it is crucial that documentation is clear, concise, and comprehensive.

Attributes of a good assessment report are listed below:

- A report should be clear and well-organised
- A high quality of writing should be maintained.
- A report should be complete in that all required information is adequately addressed.
- A report should exhibit scientific rigor.
- A report should adequately summarize critical issues and basis for regulatory decision
- A report should identify all major and critical deviations by the applicant from regulatory requirements, internal policy and/or scientific principles.
- Questions relating to deficiencies observed in an application should be clear, relevant and identify the action required from the applicant

For further information relating to the attributes above, refer to Guide for Good Review for Preparation of Quality and Bioequivalence Assessment Reports.

Procedures for document control shall be implemented by SAHPRA and should specify, based on specific criteria, who can create, revise, review and approve documents. The document management system should also ensure that documents are easily searchable and indexed but also ensure that only the right people have access to mitigate the risk of information leakage.

13 COMMUNICATION

Good communication is critical and has many advantages for SAHPRA, applicants and the public. It improves the efficiency of the review process, allowing patients faster access to important medical products.

13.1 Intra-Agency and Inter-Agency Communication

The review team's scientific assessment of an application and regulatory decision-making is a collaborative process. Open lines of communication among reviewers are critical to an efficient and thorough review. Review team members should communicate frequently to ensure that issues affecting multiple disciplines are shared early and that their implications are fully understood. The team should also engage with supervisory personnel

early and often to ensure alignment on the approach to review and to maintain awareness of issues identified during the review cycle. An effective review team maintains a strong interdependence among its members to support a collaborative and rigorous review. Review teams consist of members from many different disciplines. They may also consult representatives from other intra- or inter-center disciplines or review divisions. This underscores the need for efficient communication and teamwork during the review.

13.2 Applicant Communication

The communication between SAHPRA and applicants will be based on quality assurances. Publicly available working legal frameworks and documents such as guidelines, communications, notices, templates, forms and letters will be communicated to applicants through the SAHPRA website and other communication mechanisms.

Applicant involvement in the review process is important to good review management and helps to ensure transparency and clarity. During the review, the team should promptly communicate significant review issues to the applicant. Timely notification of issues allows the applicant to begin corrective actions, maximizes the chance for a first cycle approval, and may shorten the overall time to approval when additional review cycles are necessary. Applicants can also serve as a resource to the review team in understanding the contents of a marketing application.

13.3 Public Communication

The Authority shall communicate with the public during planning, evaluation and monitoring of regulatory activities to provide inputs on medical needs, efficacy expectations, risk tolerances and others through public meeting or representative of the public. The Authority shall also devise a mechanism whereby the public can provide input and comment on content and feasibility of proposed laws and guidelines.

14 CONDUCTING REVIEWS

SAHPRA shall follow reliance-based review approach involving categorization of applications based on foreign regulatory status of the medicinal product included in the application. SAHPRA will leverage the following review pathways:

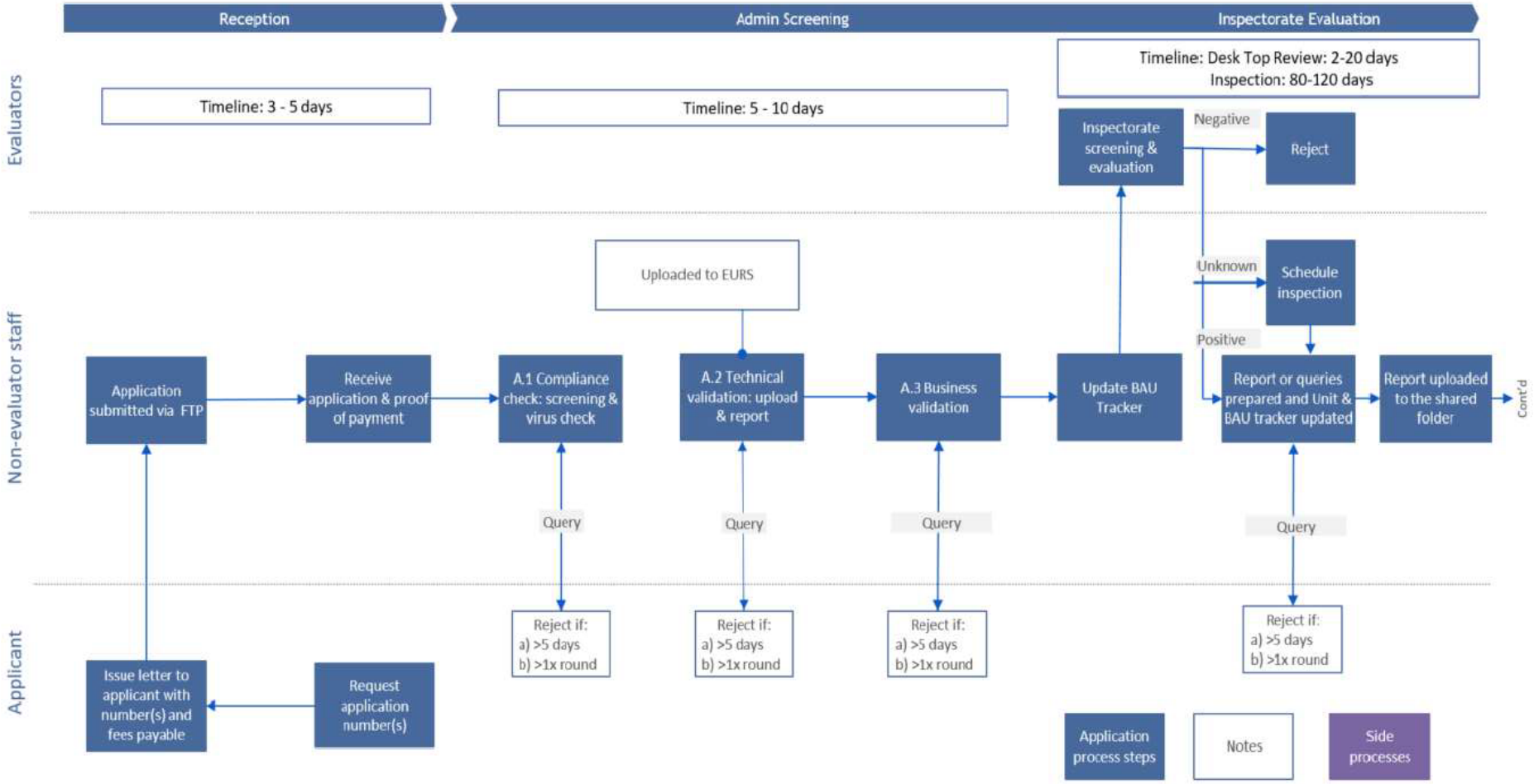
- Full Review: A comprehensive / thorough review of all aspects of the dossier, based primarily on the evaluation of data (and summaries thereof) submitted by the applicant. This is the default evaluation pathway for new registrations and variations not previously approved by SAHPRA or a RRA, or where reliance documentation provided to SAHPRA is deemed to be insufficient.
- Abridged review: A streamlined reliance-based review based primarily on unredacted assessment reports from RRAs, replacing the need to evaluate all of the data (and summaries thereof) submitted in support of an application.
- Verified review: A streamlined review based primarily on verifying, instead of evaluating, information submitted in the application against information which has already been approved by SAHPRA or an RRA.
- Recognition: A streamlined registration / approval process based on directly recognising the outcome of a review from a RRA with which SAHPRA shares a recognition agreement

Method of implementation of the review pathway shall be specific to each evaluation unit, depending on the nature of the application submitted and the resource capacity of that unit. For further information relating to implementation of review strategy, refer to unit-specific SOPs on evaluation processes.

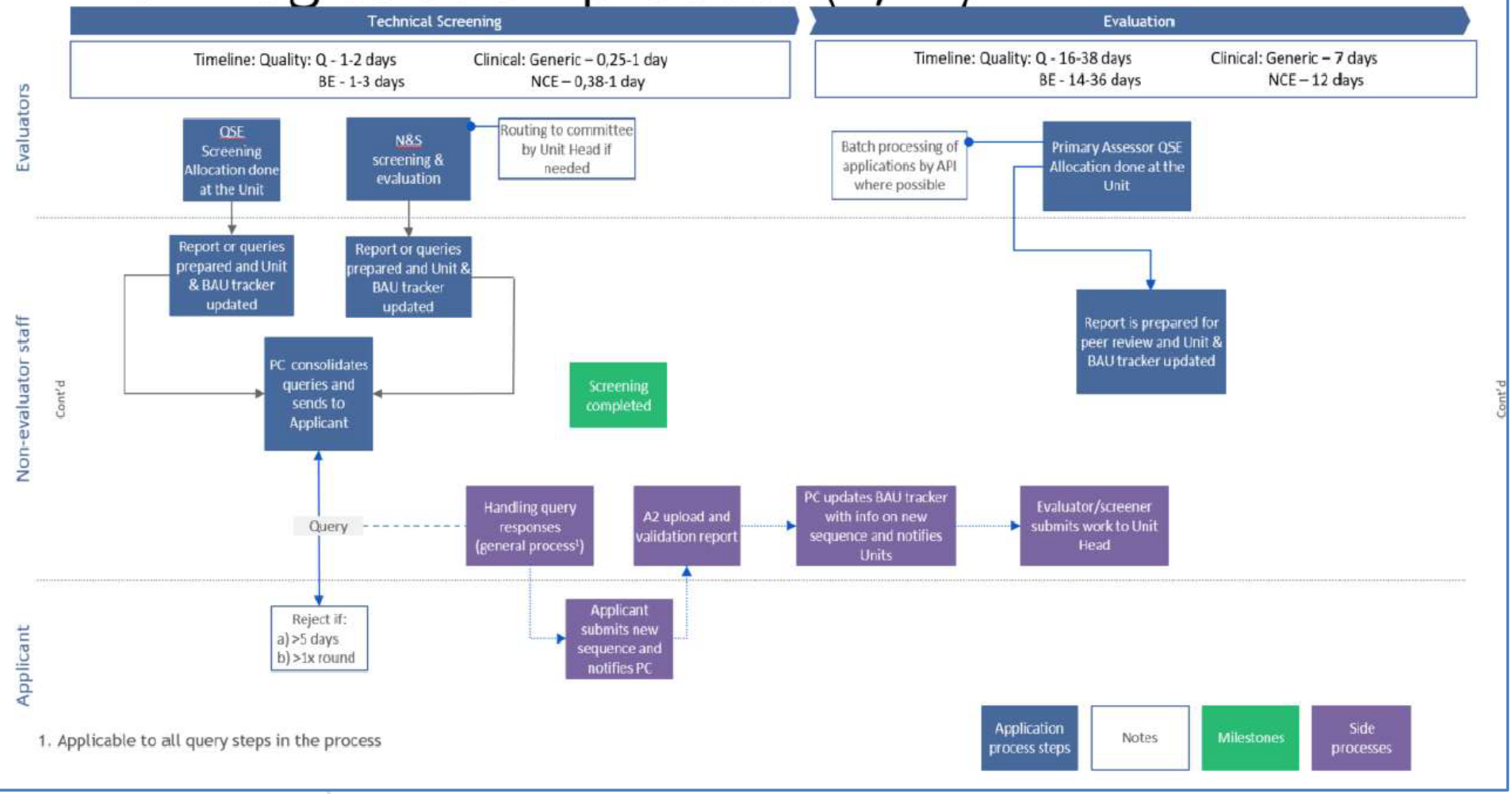
15 PROCESS MAP

15.1 BAU Registration process (see New Registration Processes below)

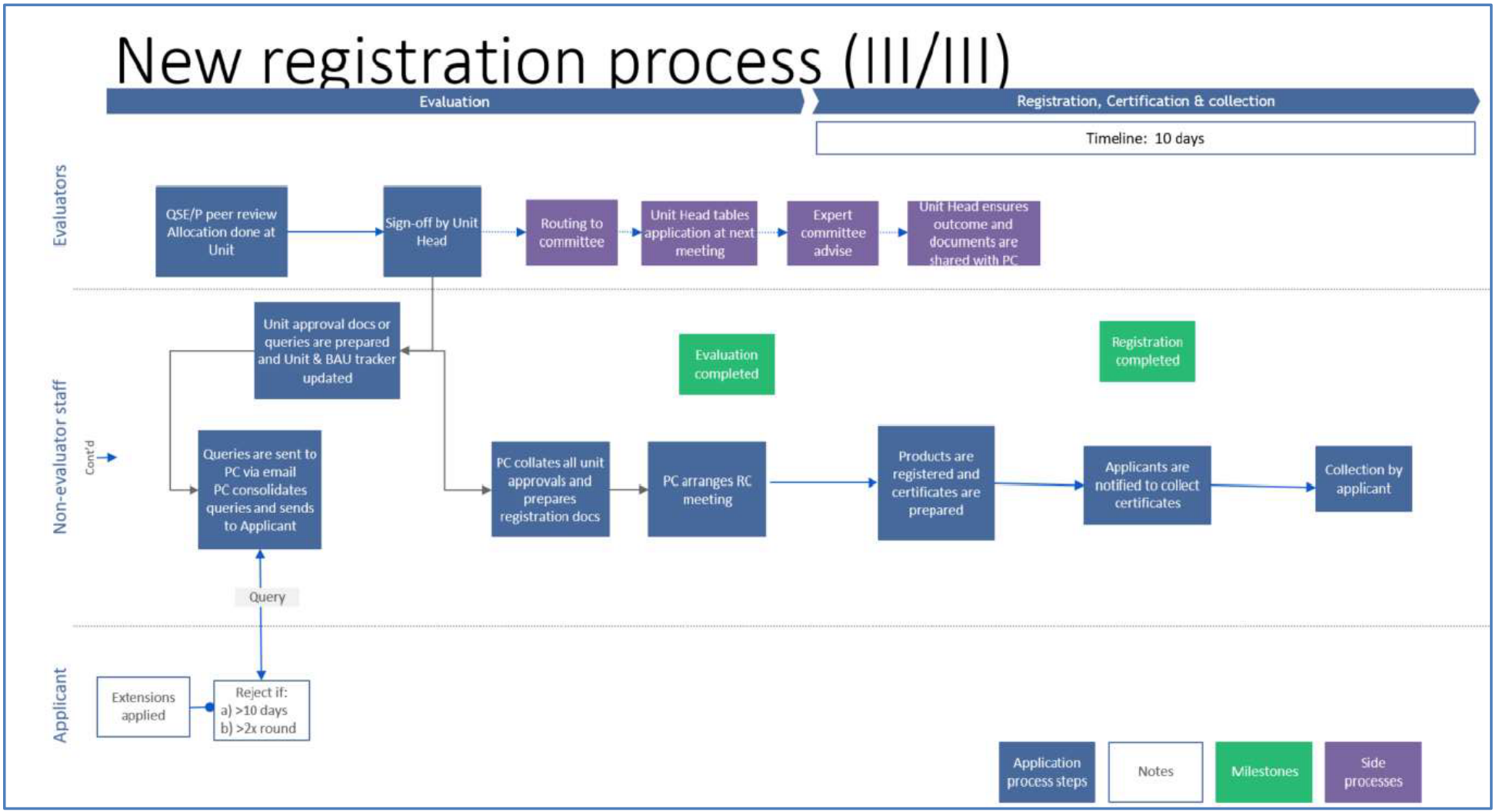
New registration process (I/III)



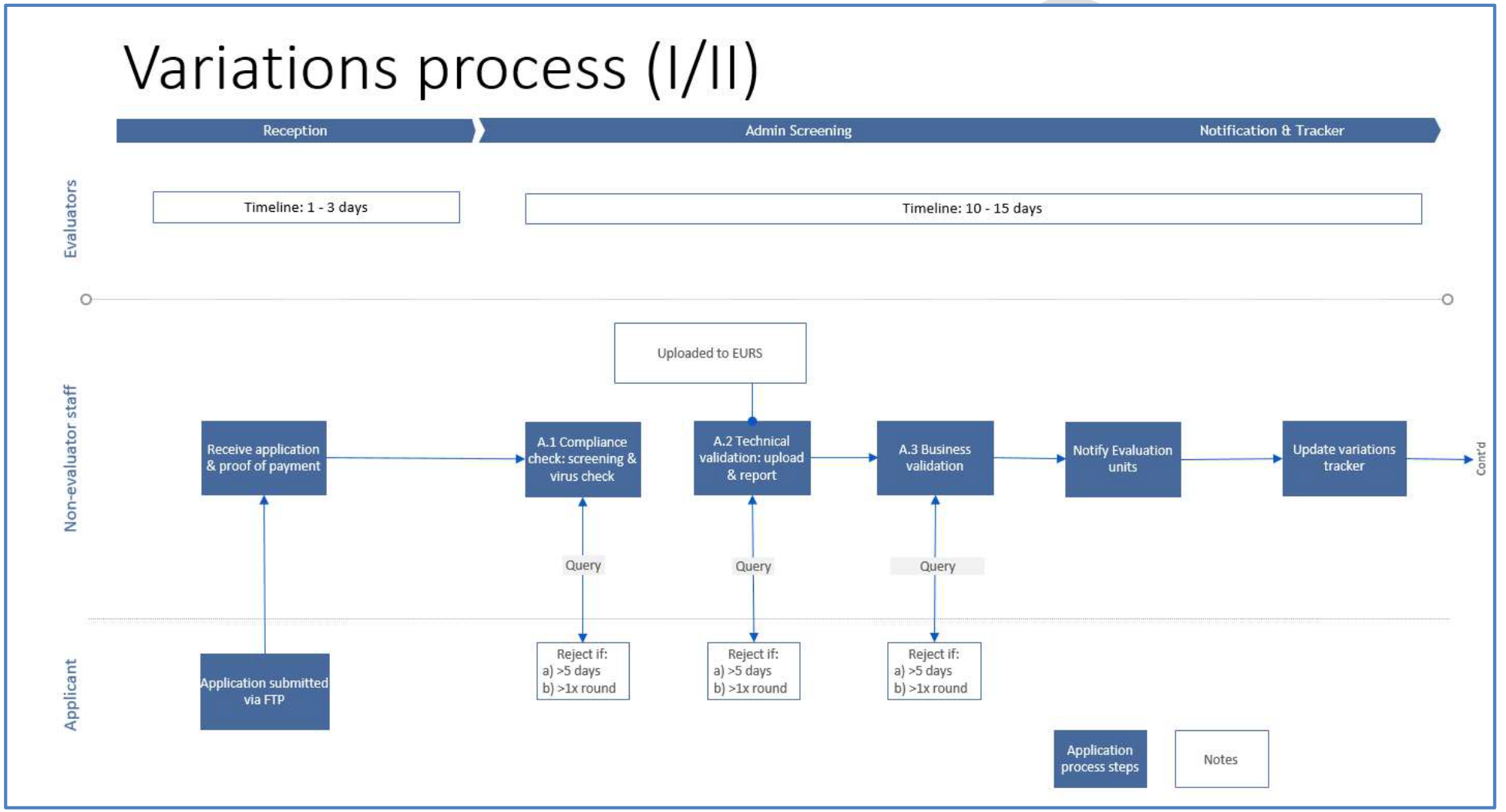
New registration process (II/III)

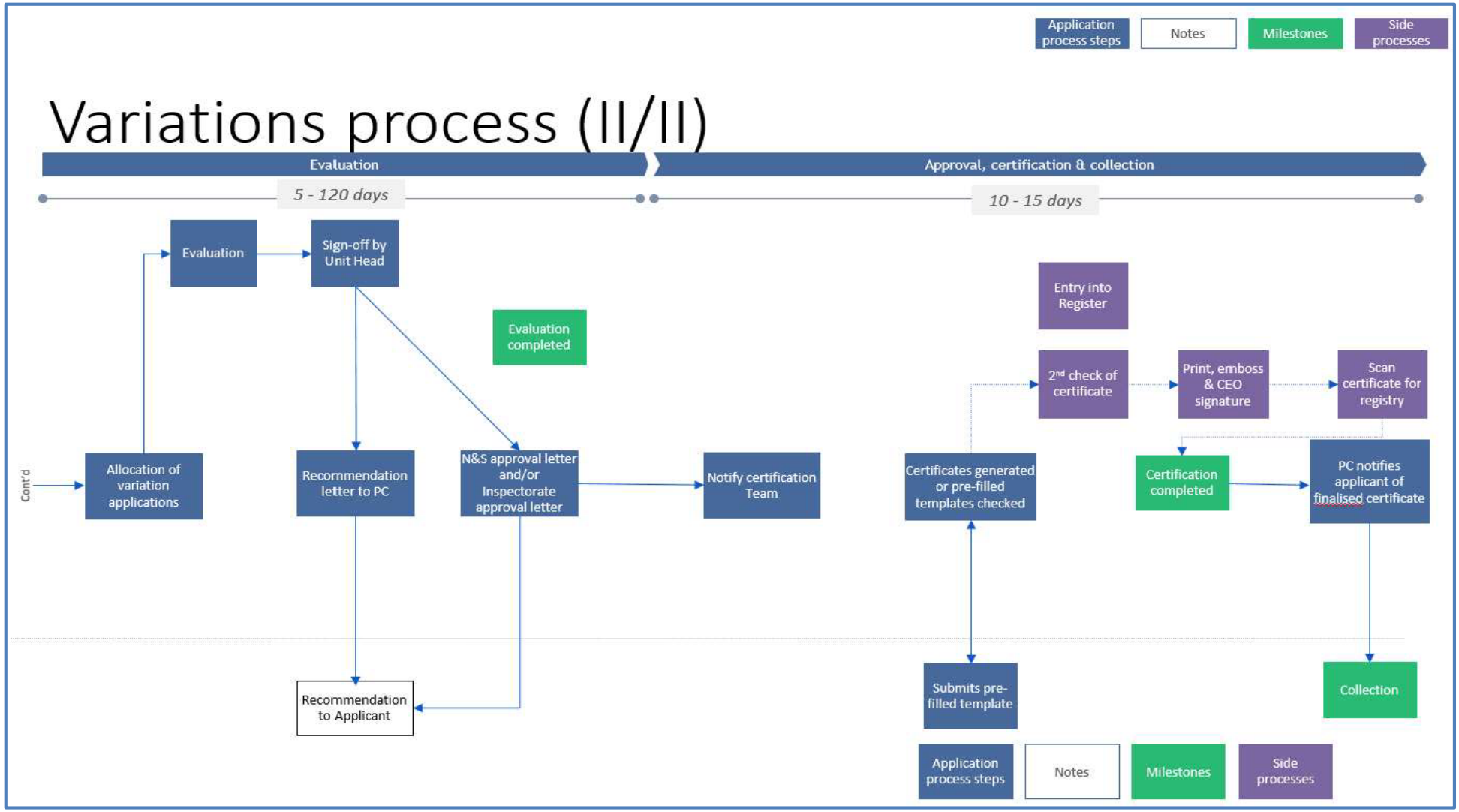


New registration process (III/III)



15.2 BAU Variation process (see Variation Processes below)




Application process steps
Notes
Milestones
Side processes
Variations process (II/II)
Evaluation
Approval, certification & collection
5 - 120 days
10 - 15 days
Evaluation
Sign-off by Unit Head
Evaluation completed
Entry into Register
2nd check of certificate
Print, emboss & CEO signature
Scan certificate for registry
Contd
Allocation of variation applications
Recommendation letter to PC
N&S approval letter and/or Inspectorate approval letter
Notify certification Team
Certificates generated or pre-filled templates checked
Certification completed
PC notifies applicant of finalised certificate
Recommendation to Applicant
Submits pre-filled template
Collection
Application process steps
Notes
Milestones
Side processes