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Review Article

Quality Control and Quality Assurance of Topical Gel Formulations: Critical Quality Attributes, Evaluation Parameters and Regulatory Considerations

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ABSTRACT

Topical gels are semisolid dosage forms used to deliver active pharmaceutical ingredients to the skin or other accessible tissues. Their quality depends on the active ingredient, gelling polymer, solvent system, pH, manufacturing process, packaging and storage conditions. Quality control (QC) evaluates materials and products against defined requirements, while quality assurance (QA) provides the wider system of procedures, documentation and review that supports consistent manufacture. This narrative review summarises QA and QC considerations for topical gels, including critical quality attributes, raw-material control, manufacturing variables, finished-product evaluation, microbiological quality, stability and regulatory guidance. Common evaluations include appearance and homogeneity, pH, rheological behaviour, assay, microbial quality and, when appropriate, in-vitro release testing. No single test can establish overall quality; methods and acceptance criteria must be justified for the particular formulation and intended use. Quality-by-design principles and risk-based thinking help connect material and process variables with measurable product attributes. ICH guidance provides general frameworks for pharmaceutical development, quality risk management, analytical procedure validation and pharmaceutical quality systems. Regulatory expectations differ by product, application pathway and jurisdiction; therefore, this review offers a practical framework rather than a universal specification for all topical gels.

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INTRODUCTION:

Topical gels are semisolid preparations in which a liquid phase is structured by a gelling agent or polymer. Depending on the active pharmaceutical ingredient (API) and formulation, they may be designed for local action on the skin or for delivery through the skin. Common ingredients include the API, gelling polymer, water or other solvents, humectants, pH-adjusting agents and, where needed, preservatives. Each ingredient serves a defined purpose, but interactions between components can influence the final product's physical properties and performance [1,2].

The manufacturing process also contributes to product quality. Incomplete polymer hydration may cause lumps or inconsistent viscosity; a change in pH may affect polymer structure, API solubility or preservative performance. Storage can influence appearance, rheology, drug distribution and microbial quality. Consequently, topical gel quality should be assessed using a product-specific combination of formulation knowledge, process controls and suitable testing rather than relying on a single result [1,3].

This review discusses practical QA and QC principles for topical gel formulations. It is a narrative overview, not a systematic review; the test panel and acceptance criteria should be established for the individual product and relevant market.

Quality assurance and quality control have complementary but distinct roles in maintaining this consistency. QA establishes the systems that govern how materials are purchased, how personnel are trained, how equipment is maintained, how manufacturing instructions are followed and how deviations are investigated. QC provides documented evidence that materials, in-process samples and finished products meet approved specifications. These activities work together: testing can identify a problem, while an effective quality system helps investigate its cause and prevent recurrence [4,5].

For topical gels, the choice of quality tests should be based on the formulation and its intended use. Appearance and homogeneity can reveal visible defects, while pH and rheological measurements help characterise the product's physical behaviour. Assay and, where relevant, uniformity testing provide information about the amount and distribution of the active pharmaceutical ingredient. Microbiological quality, preservative performance, stability and packaging compatibility may also need to be considered, particularly for water-containing formulations. In-vitro release testing can be useful for suitable development or regulatory purposes, but its design and interpretation must match the product and the question being investigated [1,3,9,11].

A scientifically justified testing strategy is more informative than applying the same test list to every gel. For example, a change in polymer grade may affect viscosity or gel structure, while a change in pH can influence polymer behaviour, drug solubility or preservative performance. These relationships support the use of risk assessment, suitable analytical procedures and defined manufacturing controls. ICH quality guidance describes general approaches to pharmaceutical development, quality risk management, analytical procedure validation and the pharmaceutical quality system; the applicable national requirements and product-specific commitments must also be considered [4–8].

Accordingly, this review brings together key considerations for raw-material control, manufacturing, finished-product evaluation, microbiological quality, stability, documentation and regulatory guidance. Its aim is to provide a practical overview of how QA and QC can be integrated throughout the topical gel lifecycle. The parameters discussed are examples for consideration rather than universal acceptance criteria; the final control strategy should be supported by formulation-specific data, relevant official standards and the requirements of the intended market [1,4,5,9,11].

2. QUALITY ASSURANCE AND QUALITY CONTROL

2.1 QUALITY ASSURANCE

QA comprises planned and systematic activities that provide confidence that materials, processes, records and decisions meet established requirements. Relevant activities may include supplier qualification, approved procedures, personnel training, equipment qualification, document control, deviation investigation, change control, batch-record review, complaint handling and

periodic product-quality review. QA does not replace testing; it helps ensure that testing and manufacturing are performed under controlled and documented conditions [4,5].

2.2 QUALITY CONTROL

QC focuses on sampling, specifications, testing, documentation and decisions relating to material or product conformity. Depending on the product, QC may assess incoming materials, process water, in-process bulk gel, finished product, packaging components and stability samples. Analytical procedures should be suitable for their intended purpose and appropriately validated or verified. ICH Q2 (R2) describes principles of analytical procedure validation, while ICH Q14 addresses science- and risk-based analytical procedure development [6,7].

2.3 INTEGRATION OF QA AND QC

An out-of-specification result should be documented and investigated through an approved procedure rather than repeatedly tested until a passing result appears. The investigation may consider sampling, method performance, laboratory practice, raw materials and manufacturing history. Any corrective or preventive action should be supported by the investigation findings and documented in the quality system [4,5].

Figure 1: QA/QC Workflow Across the Topical Gel Lifecycle

Incoming materials	Manufacturing	In-process checks	Finished-product QC	QA disposition
Identity and supplier controls	Approved process and equipment	Mixing, hydration, pH and bulk uniformity	Testing against justified specifications	Record review, deviations and release decision

Figure 1: Simplified Lifecycle Workflow. Stability Monitoring, Complaint Review and Change Control Continue After Batch Release.

3. QUALITY-BY-DESIGN AND CRITICAL QUALITY ATTRIBUTES

Quality by design (QbD) uses scientific understanding of the product and process to develop a suitable control strategy. ICH Q8 (R2) discusses pharmaceutical development; ICH Q9 (R1) describes quality risk management; and ICH Q10 sets out a pharmaceutical quality-system framework across the product lifecycle [4,5,8] These are general frameworks and do not prescribe one fixed set of tests for every topical gel.

A quality target product profile (QTPP) describes the intended product characteristics, such as dosage form, route, strength, performance, container and stability. Critical quality attributes (CQAs) are properties that should remain within suitable limits to ensure product quality. Potential CQAs for a topical gel include API identity and content, uniformity, pH, rheological behaviour, microbial quality, physical stability and drug-release performance where relevant. The final list should be justified by product knowledge, risk assessment and intended use [1,4,5].

Figure 2: Simplified QbD Framework

Define QTPP	Identify CQAs	Assess risks	Set control strategy	Review lifecycle data
Intended product and use	What must be controlled?	Material and process variables	Specifications and process checks	Trend data and continual improvement

Figure 2: Conceptual Framework; Attributes and Controls Depend on Formulation-Specific Evidence and Risk Assessment.

4. RAW MATERIALS AND MANUFACTURING CONTROLS

Raw-material controls should reflect the function and risk of each ingredient. The API requires suitable identity and quality testing. For polymers and other excipients, relevant attributes may include grade, viscosity characteristics, moisture content, microbial quality and supplier consistency. Water quality is important for water-based products, and the applicable specification should reflect the manufacturing process

and regulatory requirements. Approved suppliers, defined specifications, appropriate sampling and trend review can help detect variability before it affects production [3–5] Manufacturing instructions should define the order of addition, mixing conditions, hydration time where applicable, temperature limits, pH adjustment, deaeration, bulk hold time and filling conditions. These parameters are formulation-specific. Inadequate mixing may cause non-uniformity, while excessive mixing can introduce air or alter structure. Equipment should be suitable for the batch size and cleaned under approved procedures. In-process checks can detect developing problems before final testing.

Changes to a polymer grade, supplier, equipment, batch size or manufacturing sequence should be assessed through formal change control. Depending on risk, the assessment may lead to additional testing, qualification, stability studies or validation [4,5].

5. EVALUATION PARAMETERS FOR TOPICAL GELS

The test panel should reflect the formulation, API, intended use, claims and applicable compendial or regulatory requirements. Table 1 summarises common evaluation approaches; it is not a universal release specification. Acceptance criteria should be supported by development data, relevant official standards and product-specific regulatory commitments.

Table 1: Common Evaluation Parameters for Topical Gel Formulations.

Parameter	Purpose	Typical approach / key consideration
Appearance and homogeneity	Identify visible defects, lumps, phase separation or colour changes	Visual examination under defined conditions; microscopy where justified.
pH	Assess formulation suitability and potential effects on API, polymer or preservative	Use a calibrated pH meter with defined sample preparation and temperature.
Viscosity / rheology	Characterise consistency and batch-to-batch behaviour	Use suitable viscometer/rheometer; define geometry or spindle, speed, temperature and sample handling.
Drug content / assay	Measure API amount	Use a suitable validated method, such as HPLC or UV-visible spectroscopy when appropriate for the API and matrix.
Uniformity	Assess whether API distribution is consistent	Use a justified sampling plan and method capable of recovering and quantifying the API.
Microbiological quality	Assess compliance with applicable microbial limits and preservation requirements	Use relevant pharmacopoeial or jurisdictional methods; requirements depend on product category.
In-vitro release testing	Compare release behaviour when relevant to development or regulatory submission	Justify apparatus, membrane, receptor medium, sampling and analytical method.
Stability	Monitor quality attributes over time	Assess relevant physical, chemical and microbiological properties in suitable packaging.
Packaging compatibility	Assess product–container interaction and dispensing performance	Evaluate leakage, sorption, water loss, compatibility and functionality as relevant.

5.1 Appearance, homogeneity and pH

Appearance checks can identify visible defects such as particles, phase separation, discolouration or air pockets. Visual inspection may not detect every form of API non-uniformity, so additional assessment should be considered when justified. pH should be measured with a calibrated instrument and consistent procedure. A pH range should be based on product stability, performance and safety data rather than copied from unrelated formulations.

5.2 VISCOSITY AND RHEOLOGICAL BEHAVIOUR

Viscosity is often monitored as an indicator of gel consistency, but one value may not fully describe a non-Newtonian semisolid. Results depend on instrument, spindle or geometry, speed, temperature, preshear, rest time and sample loading. These conditions should be defined and recorded to support meaningful comparison between batches and time points. Spreadability or extrusion testing may provide additional information when relevant, but the procedure also needs standardisation [1,2].

5.3 DRUG CONTENT AND ANALYTICAL METHODS

An assay should be sufficiently selective to measure the API in the presence of excipients and, where relevant, degradation products. Extraction and recovery from the gel matrix require attention because polymers and other ingredients may interfere with sample preparation or measurement. Validation characteristics should match the intended use of the method and be justified according to ICH Q2 (R2); ICH Q14 provides principles for analytical procedure development [6,7].

5.4 IN-VITRO RELEASE TESTING

In-vitro release testing may help compare formulations, assess manufacturing changes or support certain regulatory submissions. It should not automatically be treated as a direct substitute for clinical performance. Apparatus, membrane, receptor medium, temperature, dose application, sampling and analytical method should be justified. The US FDA has issued specific guidance for IVRT studies for topical drug products submitted in abbreviated new drug applications; this scope should not be generalised to every topical gel [9].

5.5 MICROBIOLOGICAL QUALITY AND PRESERVATION

Water-containing gels may support microbial growth if formulation design, raw materials, manufacturing hygiene or packaging controls are inadequate. Microbial limits and preservative effectiveness testing should be selected according to product category, applicable compendial requirements and intended use. Preservative concentration alone does not establish adequate protection because pH, excipient interactions, packaging and manufacturing practices can influence performance.

6. STABILITY AND PACKAGING

Stability studies evaluate whether relevant quality attributes remain acceptable over the proposed shelf life. For topical gels, useful measurements may include appearance, pH, viscosity or rheology, assay, degradation products, microbial quality, release performance where justified and packaging integrity. Conditions, time points and acceptance criteria should follow applicable guidance and product characteristics. ICH Q1A (R2) provides a general framework for stability testing of new drug substances and products, but applicability and regional requirements should be confirmed [10].

Packaging is part of the product system. The container may influence water loss, light or oxygen exposure, API sorption, microbial protection and ease of dispensing. Stability studies should therefore use packaging representative of the proposed market pack. Packaging changes should be assessed for compatibility and performance risks.

7. DOCUMENTATION, DEVIATIONS AND CONTINUAL IMPROVEMENT

Good documentation supports traceability from incoming materials through manufacturing, testing, review and distribution. Records should make it possible to determine what was done, by whom, using which materials and equipment, and whether approved requirements were met. Data should be attributable, legible, contemporaneous, original or a verified true copy, accurate, complete and protected against unauthorised alteration.

Deviations, out-of-specification results, complaints and recurring trends should be investigated through approved procedures. Corrective and preventive actions should address supported causes rather than only the immediate symptom. Periodic review of batch results, stability data, complaints and changes may reveal patterns that individual batch review cannot show. These practices align with the lifecycle concepts in ICH Q10 [5].

8. REGULATORY CONSIDERATIONS

Requirements vary by country, product classification, application pathway and intended claims. Applicable pharmacopoeias, national GMP rules, approved specifications and application-specific guidance should be checked before finalising a test plan. ICH guidelines provide harmonised principles but do not replace local law or product-specific commitments [4,8,10].

Table 2: Selected Guidelines Relevant to Topical Gel Development and Quality Management.

Guideline / source	Relevance	Scope note
ICH Q8(R2): Pharmaceutical Development	Development rationale and product/ process understanding	General development framework.
ICH Q9(R1): Quality Risk Management	Risk assessment, control, communication and review	Use to prioritise controls based on scientific knowledge and risk.
ICH Q10: Pharmaceutical Quality System	CAPA, change management and lifecycle quality system	Applies across relevant lifecycle stages.
ICH Q2(R2): Validation of Analytical Procedures	Validation principles for analytical methods	Validation should fit the method's intended use.
ICH Q14: Analytical Procedure Development	Science- and risk-based analytical method development	Supports procedure development and lifecycle management.
ICH Q1A(R2): Stability Testing	General principles for stability study design	Confirm product and regional applicability.
US FDA topical IVRT guidance	IVRT studies for topical products in ANDA submissions	Application-specific, not universal for all topical gels.
US FDA topical Q3 guidance	Physicochemical and structural characterization in ANDA submissions	Do not present as a universal routine QC checklist.

ICH lists Q2 (R2), Q8 (R2), Q9 (R1), Q10 and Q14 within its quality guideline framework [4–8]. The FDA topical Q3 guidance should be discussed only within its stated scope of physicochemical and structural characterization for ANDA submissions [11].

9. COMMON QUALITY RISKS AND EXAMPLE CONTROLS

The examples in Table 3 illustrate possible links between a quality risk, its potential impact and a control strategy. They should be adapted through a product-specific risk assessment.

Table 3: Example Quality Risks and Possible Controls for Topical Gels.

Potential quality risk	Possible quality impact	Example control strategy
Polymer or excipient lot variability	Changes in gel formation, viscosity or stability	Supplier qualification, incoming-material specifications and lot-trend review.
Incomplete hydration or inadequate mixing	Lumps, non-uniformity or variable rheology	Defined order of addition, mixing conditions, hydration time and in-process checks.
Uncontrolled pH adjustment	Changes in viscosity, API solubility or preservative performance	Controlled pH adjustment, calibrated pH meter and justified acceptance limits.
Entrapped air or inadequate deaeration	Appearance defects and filling variability	Defined deaeration procedure and bulk inspection.
Microbial contamination	Product deterioration and potential user risk	Hygienic manufacture, water-system controls, microbial testing and preservation assessment.
API crystallisation or physical change	Changes in appearance, stability or release behaviour	Risk-based microscopy or other suitable assessment and stability monitoring.

Potential quality risk	Possible quality impact	Example control strategy
Packaging interaction or water loss	Changes in concentration, texture or delivered quantity	Container-closure compatibility and stability studies in representative packaging.
Uncontrolled process or supplier change	Batch variability and inconsistent quality	Formal change control and additional qualification or validation where justified.

10. CHALLENGES AND FUTURE PERSPECTIVES

A key challenge is that semisolid formulations can respond to small changes in material properties and processing conditions. A method suitable for one polymer or API may not be appropriate for another. Rheological results depend on measurement conditions, while tests such as spreadability and IVRT may be difficult to compare if procedures are not standardised. This supports product-specific method development, justified acceptance criteria and transparent documentation.

Future work may improve rheological characterisation, develop more discriminating in-vitro performance methods, strengthen risk-based process monitoring and make better use of stability and batch-trend data. Digital documentation and process analytical technologies may help detect variation when their use is justified and appropriately controlled.

CONCLUSION

Reliable topical gel quality depends on formulation design, controlled manufacture, suitable testing and an effective pharmaceutical quality system. QA establishes systems for consistent and documented work, while QC provides measurements against defined requirements. A suitable quality strategy links product-specific CQAs with material controls, in-process monitoring, appropriate analytical procedures, microbiological safeguards, stability assessment and packaging. ICH guidance offers structured principles for development, risk management, analytical procedures and lifecycle quality management; final specifications and regulatory commitments must nevertheless reflect the individual product and target market.

12. REVIEW APPROACH AND SCOPE

This article was prepared as a narrative review of quality assurance and quality control considerations for topical gel formulations. The existing reference list was used as the starting point, and additional peer-reviewed literature and regulatory guidance were consulted to clarify current issues in semisolid product characterization. The material was organized around formulation and process variables, critical quality attributes, routine testing, analytical procedures, stability, and regulatory considerations. The purpose is to connect these topics in a practical way for pharmacy students and readers who are beginning to study topical product

quality. A narrative review does not use the same predefined screening, duplicate independent assessment, and formal risk-of-bias procedures as a systematic review. Therefore, this article should not be interpreted as an exhaustive or quantitative synthesis of every published study. The discussion is intended to summarize recurring principles and examples. Where a recommendation depends on product classification or jurisdiction, the applicable official guidance and approved product requirements should take priority over a general statement in this review. The need for product-specific assessment is particularly important for semisolid formulations because two products described as gels may differ in composition, microstructure, rheological behaviour, and performance [1,3,12,14].

13. CRITICAL MATERIAL ATTRIBUTES AND CRITICAL PROCESS PARAMETERS

The quality of a finished gel is influenced by the properties of the materials used and by the conditions under which the formulation is manufactured. Critical material attributes may include the grade and viscosity characteristics of a polymer, the particle size or physical state of a suspended drug, the quality of water, and the functional characteristics of preservatives or other

excipients. These attributes should be selected according to the formulation rather than treated as an identical checklist for every gel. Supplier qualification and incoming-material testing help confirm that materials are suitable and consistent with the approved specification [3,5]. Critical process parameters may include the order of addition, mixing speed and duration, hydration time, temperature, pH adjustment, deaeration, bulk holding time, and filling conditions. For example, a polymer may not hydrate completely if the addition sequence or mixing conditions are unsuitable. This can lead to lumps, local differences in viscosity, or an uneven appearance. Conversely, an excessive mixing step may introduce air or alter the structure of a sensitive formulation. Such examples show why in-process checks are valuable: they can identify developing variation before the batch reaches final-product testing. A practical control strategy links the material or process variable to the quality attribute that it may affect. The relationship should be supported by development data, risk assessment, and experience with the formulation. Design-of-experiments approaches can help evaluate several variables together when a formulation is being developed or optimised. However, a statistical design is useful only when the selected factors, responses, and experimental range are scientifically justified. ICH Q8 (R2), Q9 (R1), and Q10 provide general frameworks for development, risk management, and the pharmaceutical quality system; they do not prescribe universal process settings for all topical gels [4,5,8].

14. RHEOLOGY, MICROSTRUCTURE AND PRODUCT PERFORMANCE

Rheological behaviour is an important part of the characterization of topical gels because it describes how the material flows or deforms when force is applied. A single viscosity value may not fully represent a semisolid product. Some formulations show shear-thinning behaviour, yield stress, thixotropy, or changes in structure after rest. Results can also depend on the instrument, spindle or geometry, measurement speed, temperature, sample loading, and the time allowed for the sample to equilibrate. These conditions should therefore be specified and kept consistent when comparing batches or stability samples [1,2,12]. Microstructure can provide additional information about the arrangement of the formulation and the physical state of its components. Depending on the product, relevant observations may include the presence of crystals, dispersed particles, droplets, or structural differences seen by suitable microscopy or other methods. The selection of a method should be based on the question being asked and on whether the method can produce reliable, interpretable data. The FDA's final Q3 guidance, issued in March 2026, describes physicochemical and structural characterization for certain topical products submitted in abbreviated new drug applications. Its purpose is to support dosage-form characterization and assessment of properties potentially relevant to bioequivalence; it should not be described as a universal routine quality-control checklist for every gel [11,13]. The product may also change after it is applied to the skin. Evaporation of volatile components, changes in concentration, crystallization, and changes in rheological properties can alter the formulation's state during use. This is one reason why the properties measured in a sealed container may not describe every aspect of behaviour after application. The review by Jin and colleagues discusses such changes in topical semisolid products, while later work has examined rheological behaviour under in-use conditions [1,12]. These considerations support a broader evaluation strategy in which routine release tests are supplemented, where justified, by methods that address the product's intended performance.

15. METHOD SUITABILITY, VALIDATION AND DATA INTEGRITY

A test result is useful only when the analytical procedure is suitable for its intended purpose. For drug-content testing, the sample preparation should recover the active ingredient from the gel matrix, and excipients should not cause unacceptable interference. The method should be evaluated for relevant characteristics such as specificity, accuracy, precision, range, and other performance parameters according to the intended use. ICH Q2 (R2) describes general principles for validation of analytical procedures, while ICH Q14 discusses science- and risk-based development of analytical procedures [6,7]. For physical tests, method conditions also need to be controlled. A pH

measurement should use a suitable calibrated meter and a defined sample-handling procedure. Rheological measurements should state the instrument configuration and test conditions. In-vitro release testing should define the apparatus, membrane where used, receptor medium, temperature, sample application, sampling schedule, and analytical method. Results from different laboratories or formulations may not be directly comparable if these details differ. A method transfer or change in equipment may therefore require documented assessment to determine whether the procedure remains fit for purpose. Data integrity is another essential part of reliable quality decisions. Records should be attributable, legible, contemporaneous, original or a verified true copy, accurate, complete, and protected from inappropriate alteration. Unusual results should be investigated through an approved procedure, with attention to the method, instrument, sample, analyst, and manufacturing history. Repeating tests without a scientifically justified investigation can obscure rather than resolve the cause of a result. The quality system should document the investigation, conclusion, and any corrective or preventive action [5,7].

16. STABILITY-INDICATING CONTROL STRATEGY

Stability assessment should consider the changes that are reasonably likely to affect a topical gel throughout its proposed shelf life. These may include changes in appearance, pH, rheological properties, drug content, degradation products, microbial quality, release behaviour where justified, and packaging integrity. The exact test panel and study conditions should reflect the formulation, container, intended storage conditions, and applicable regulatory commitments. ICH Q1A (R2) provides a general framework for stability testing of new drug substances and products, but the relevant regional requirements should be confirmed for the specific application [10]. For gels, physical instability can be as important as chemical degradation. A product may show phase separation, syneresis, changes in consistency, crystal formation, or loss of homogeneity even when the assay remains within its acceptance criteria. Therefore, stability evaluation should not rely on drug content alone. Packaging should also be considered because the container can influence water loss, exposure to light or oxygen, product sorption, microbial protection, and dispensing. Stability studies should use packaging representative of the intended market pack, and a proposed packaging change should be assessed for its potential effect on product quality. Accelerated studies can provide useful information about likely changes under elevated stress conditions, but they should not automatically be treated as a replacement for appropriate long-term data. The interpretation depends on the product and the study design. A clear protocol, predefined acceptance criteria, documented observations, and appropriate trend analysis help make the resulting evidence more meaningful. For a semisolid formulation, combining chemical, physical, microbiological, and packaging observations gives a more complete picture of stability than focusing on a single parameter [10,14].

17. PRACTICAL RECOMMENDATIONS FOR A PRODUCT-SPECIFIC CONTROL PLAN

A practical control plan should begin with the intended use and the known characteristics of the formulation. The team should identify which attributes are important to product quality, determine how those attributes may vary, and select tests or process controls that can detect meaningful variation. The plan should also distinguish tests needed for routine batch release from tests used during formulation development, stability studies, process validation, or a regulatory comparison. Not every useful development test must become a routine release test, and not every routine test is sufficient to establish product performance on its own [3,5,11]. The following sequence can be used as a starting point for discussion. It is not a universal specification, and each step should be adapted to the product and applicable standards: 1. Define the product's intended use, dosage form, strength, packaging, and target market. 2. Identify relevant material attributes and process variables through formulation knowledge and risk assessment. 3. Select methods for identity, assay, pH, rheology, uniformity, microbiological quality, stability, and other relevant attributes. 4. Establish justified procedures and acceptance criteria using development data, validated or verified methods, and official requirements where applicable. 5. Document incoming-material decisions,

in-process checks, deviations, out-of-specification investigations, batch review, and change control. 6. Review trends from manufacturing, laboratory testing, stability, complaints, and changes to determine whether the control strategy remains effective. A control plan should be reviewed when new evidence becomes available or when a significant change is proposed. Examples include a new polymer supplier, a change in batch scale, a modified manufacturing sequence, a new container, or a revised analytical procedure. The level of additional testing should be proportionate to the assessed risk and supported by documented reasoning. This approach connects the technical tests described in this review with the wider purpose of QA: preventing avoidable variation and maintaining a consistent, evidence-based quality system [4,5,8].

18. LIMITATIONS AND FUTURE DIRECTIONS

The literature and regulatory examples discussed in this review indicate that topical gel quality cannot be described adequately by one test or one fixed list of acceptance criteria. Formulations differ in their active ingredients, polymers, excipients, physical structure, packaging, and intended use. In addition, some regulatory recommendations are written for particular product categories or application pathways. For this reason, the guidance discussed here should be applied within its stated scope and should not be assumed to replace local requirements or product-specific commitments [1,3,11]. A further limitation is that this is a narrative review rather than a systematic review with a registered protocol and formal risk-of-bias assessment. It therefore provides a practical overview but does not claim to identify every relevant publication or quantify the strength of evidence across all methods. Future reviews could use a reproducible database search, explicit inclusion and exclusion criteria, and structured appraisal of the evidence on gel-specific quality attributes. More comparative work would also be useful to understand how measurement conditions affect reproducibility between laboratories. Future development may benefit from improved and better standardised rheological methods, more informative characterization of microstructure, and carefully justified in-vitro performance tests. Digital records and process analytical technologies may support monitoring where they are appropriately validated and integrated into the quality system. However, new technologies should be adopted because they answer a defined quality question and improve understanding or control, not simply because they are available. The central requirement remains a scientifically justified, product-specific approach supported by reliable data and clear documentation [7,11,14].

REFERENCES

1. Jin X, Imran M, Mohammed Y. Topical semisolid products—understanding the impact of metamorphosis on skin penetration and physicochemical properties. Pharmaceutics. 2022;14 (11):2487. doi:10.3390/pharmaceutics14112487. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC9692522/
2. Szoleczky R, Budai-Szűcs M, Csányi E, Berkó S, Tonka-Nagy P, Csóka I, et al. Analytical Quality by Design (AQbD) approach to the development of in vitro release test for topical hydrogel. Pharmaceutics. 2022;14 (4):707. doi:10.3390/pharmaceutics14040707. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC9026520/
3. Namjoshi S, Dabbaghi M, Roberts MS, Grice JE, Mohammed Y. Quality by Design: development of the Quality Target Product Profile (QTPP) for semisolid topical products. Pharmaceutics. 2020;12 (3):287. doi:10.3390/pharmaceutics12030287. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC7150996/
4. International Council for Harmonisation (ICH). Pharmaceutical development Q8 (R2). 2009. Available from: https://database.ich.org/sites/default/files/Q8_R2_Guideline.pdf
5. International Council for Harmonisation (ICH). Pharmaceutical quality system Q10. 2008. Available from: https://database.ich.org/sites/default/files/Q10_Guideline.pdf

6. International Council for Harmonisation (ICH). Validation of analytical procedures Q2 (R2). Step 4. 2023 Nov 1. Error-corrected guideline, 2025. Available from: https://database.ich.org/sites/default/files/ICH_Q2%28R2%29_Guideline_2023_1130_ErrorCorrection_2025.pdf
7. International Council for Harmonisation (ICH). Analytical procedure development Q14. Step 4. 2023 Nov 1. Error-corrected guideline, 2025. Available from: https://database.ich.org/sites/default/files/ICH_Q14_Guideline_2023_1130_ErrorCorrection_2025.pdf
8. International Council for Harmonisation (ICH). Quality risk management Q9 (R1). Step 4. 2023 Jan 18. Available from: https://database.ich.org/sites/default/files/ICH_Q9%28R1%29_Guideline_Step4_2023_0126_0.pdf
9. U.S. Food and Drug Administration. In vitro release test studies for topical drug products submitted in ANDAs: guidance for industry. 2022 Oct. Draft guidance; not for implementation. Available from: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/in-vitro-release-test-studies-topical-drug-products-submitted-andas
10. International Council for Harmonisation (ICH). Stability testing of new drug substances and products Q1A (R2). Step 4. 2003 Feb 6. Available from: https://database.ich.org/sites/default/files/Q1A_R2_Guideline.pdf
11. U.S. Food and Drug Administration. Physicochemical and structural (Q3) characterization of topical drug products submitted in ANDAs: guidance for industry. 2026 Mar. Final guidance. Available from: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/physicochemical-and-structural-q3-characterization-topical-drug-products-submitted-andas
12. U.S. Food and Drug Administration. SUPAC-SS: nonsterile semisolid dosage forms—scale-up and postapproval changes: chemistry, manufacturing, and controls; in vitro release testing and in vivo bioequivalence documentation. 1997 May. Available from: https://www.fda.gov/media/71141/download
13. Chiarentin L, Cardoso C, Miranda M, Vitorino C. Rheology of complex topical formulations: an analytical Quality by Design approach to method optimization and validation. Pharmaceutics. 2023;15 (7):1810. doi:10.3390/pharmaceutics15071810. Available from: https://www.mdpi.com/1999-4923/15/7/1810
14. Badruddoza AZM, Yeoh T, Shah JC, Walsh T. Assessing and predicting physical stability of emulsion-based topical semisolid products: a review. J Pharm Sci. 2023;112 (7):1772-1793. doi:10.1016/j.xphs.2023.03.014.

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