

Blood-Contacting Photopolymer Devices: Haemocompatibility, Surface State, Flow, Thrombosis and Sterilisation

A finished-device framework for blood-interaction qualification under clinically representative flow

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Abstract

Haemocompatibility is a system property of a finished blood-contacting device, the blood population and the imposed flow history. It cannot be inferred from cytotoxicity, resin designation, a low static platelet count or one haemolysis result. Vat-photopolymerised devices introduce coupled variables: conversion and extractables, pixel- and layer-scale topography, inaccessible wash domains, finishing residues, wettability, sterilisation-induced change, geometric flow disturbance and time-dependent surface conditioning by plasma proteins. This review defines a non-compensatory qualification architecture for blood-contacting photopolymer devices. It begins with contact classification and a frozen finished-device state, then links surface chemistry and morphology to protein adsorption, platelets, coagulation, complement, leucocytes, haemolysis and thrombosis under relevant flow. Static screening is separated from dynamic and in vivo evidence. Blood source, anticoagulant, collection-to-test time, shear field, controls and drug exposure are treated as controlled inputs. Sterilisation is a material-processing step requiring post-sterilisation verification rather than a label added after testing. The result is a device-specific evidence matrix with explicit residual uncertainty, without disclosing proprietary formulations or establishing universal acceptance limits. Keywords: haemocompatibility; photopolymer; blood-contacting device; thrombosis; haemolysis; platelet activation; flow; sterilisation

1. Significance, scope and ownership

ISO 10993-4:2017 establishes the current published framework for selecting tests for medical-device interactions with blood [1]. Its 2025 amendment forms part of the applicable controlled record [2]. ISO 10993-1:2025 places biological evaluation inside risk management and requires evidence appropriate to the final device and intended contact [3]. A draft replacement for Part 4 exists, but a draft is not treated here as a published requirement.

1.1 Corpus boundary

ER-257 owns blood-contact classification, surface-blood mechanisms, dynamic flow qualification, thrombosis, haemolysis and sterilisation effects for blood-contacting photopolymer devices. ER-175 retains washing-system engineering; ER-181 retains post-cure engineering; ER-206 retains micro-computed-tomography metrology; ER-228 retains general antifouling surfaces; ER-251 owns biological-evaluation planning; ER-252 owns cytotoxicity-test artefacts; ER-253 owns analytical evaluation thresholds; ER-254 owns constituent toxicological risk; ER-255 and ER-256 own skin and mucosal contact; ER-258 owns bone-implant interfaces; ER-259 owns antimicrobial-claim durability; and ER-260 owns patient-specific traceability. None of those reviews substitutes for blood-interaction evidence.

2. Classify the blood-contacting use

Define whether contact is indirect, external communicating or implanting; the anatomical circuit; contact duration; blood volume; flow range; recirculation; temperature; and whether the device contacts whole blood, plasma or a cellular fraction. Record intended anticoagulation or antiplatelet therapy, patient population and foreseeable deviations. The same coupon can be irrelevant to a catheter lumen, oxygenator pathway or implant because the ratio of surface to blood volume, residence time and shear history differ. Classification determines the biological questions; it does not automatically select a universal panel.

3. Freeze the finished-device state

Record resin lot, printer, wavelength, layer schedule, build orientation, supports, wash solvent and renewal, drying, post-cure dose and temperature, machining, polishing, coating, cleaning, packaging, ageing and sterilisation. Include internal channels and support-removal scars in the represented state. Blood tests performed on smooth moulded plaques do not qualify a printed device when the actual lumen contains layer cusps, trapped residues or different conversion. Coupons are acceptable only when their chemistry, topography, processing and sterilisation conservatively represent all relevant device surfaces.

4. Characterise the surface presented to blood

Measure topography at scales relevant to proteins, cells and flow; report areal roughness, defect population and directional structure rather than one line-average value. Characterise wettability after equilibration, surface chemistry, extractable residue, charge where relevant, coating thickness and stability.

Surface state changes after hydration and plasma conditioning. Gegenschatz-Schmid, Buzzi, Grossmann, Roschitzki, Urbanet, Heuberger, Glück, Zucker and Ehrbar showed with treated Nitinol that altered surface chemistry changed adsorbed-protein patterns and reduced thrombus formation in static and Chandler-loop tests [5]. That result is not transferable to photopolymers, but it demonstrates why nominal bulk composition is insufficient.

5. Establish the flow field

Map expected flow rate, pressure, pulsatility, residence time, recirculation, stagnation, separation, jets and wall shear. Computational predictions require mesh, rheology, boundary-condition and sensitivity records, followed by experimental confirmation at discriminating locations. For steady laminar flow of a Newtonian fluid through a circular tube, a reference wall-shear estimate is $\tau_{\text{w}} = 4 \mu Q / (\pi R^3)$ where τ_{w} is wall shear stress, μ is dynamic viscosity, Q is volumetric flow rate, and R is tube radius. This relation is a transparent reference case, not a model for pulsatile, non-Newtonian blood in complex printed geometry. Gao, Ding, Huan, Zhou, Mi and Li demonstrated shear-dependent platelet aggregation in a microfluidic flow platform [6]. Their platform is not a device-qualification method, but the result supports explicit control of haemodynamic context.

6. Control blood collection and handling

Predefine species or human donor population, inclusion criteria, number of donors, fasting or medication restrictions, collection system, needle gauge, discard volume, anticoagulant and concentration, storage temperature, mixing, transport, collection-to-test time and pooling policy. Record haematocrit,

platelet count and relevant baseline markers. Blood is a variable reagent. Donor effects, anticoagulant choice and delayed testing can obscure or imitate device effects. Replication should distinguish technical repeats from independent donors.

7. Design controls and comparators

Use a negative control with established low activation, a positive control that challenges the endpoint, and a legally marketed or otherwise justified device comparator when appropriate. Controls must experience the same blood lot, circuit, exposure time and analysis. Comparator similarity should cover contact category, flow, surface area, material state and clinical function. A comparator cannot compensate for an unrepresentative test article or an insensitive assay.

8. Resolve early protein adsorption

Measure total adsorption only when it is mechanistically useful. Prefer endpoint-specific information such as fibrinogen conformation, albumin displacement, contact-system proteins and complement deposition. Preserve the sequence from clean surface to conditioned film because early competitive adsorption can determine subsequent cell response. Hydrophilicity alone is not a haemocompatibility claim. Chemistry, hydration structure, nanoscale organisation and adsorbed-protein conformation can produce different outcomes at similar contact angles.

9. Evaluate platelets as activation, not only count

Combine adherent platelet number with morphology, activation markers, soluble release and aggregate formation. Analyse representative high-shear, low-shear and recirculation regions. Imaging should state field selection, segmentation and blinding. Almeida, Rosa, Pinto Junior, Escobar da Silva, Miguel and Oliveira printed PHEMA-polysilsesquioxane constructs with controllable nitric-oxide release and reported low platelet adhesion, with further reduction at the highest loading [4]. The study is material-specific and does not establish clinical haemocompatibility, but it directly demonstrates that printed network composition, swelling and bioactive release can alter platelet response.

10. Evaluate coagulation and thrombosis

Select markers that resolve initiation, amplification and final thrombus burden. Candidate measures include thrombin generation, thrombin-antithrombin complexes, fibrin deposition, contact-pathway activation and macroscopic or volumetric thrombus. Report whether the circuit itself activates coagulation. Static clotting time cannot represent geometry-driven deposition. Dynamic loops or flow chambers should reproduce relevant residence time and surface-to-volume ratio, and in vivo studies should be considered when bench methods cannot resolve the clinical mechanism.

11. Evaluate haemolysis

Separate material-induced from mechanically induced haemolysis. Characterise free haemoglobin, total haemoglobin and sample interference; inspect pump, connectors, temperature and air-blood interfaces. A photopolymer may contribute through chemistry, roughness or flow disturbance even when each factor alone appears small. A normalised spectrophotometric result can be represented as $H_{norm} = 100 (OD_s - OD_{neg}) / (OD_{pos} - OD_{neg})$ where H_{norm} is normalised haemolysis response, OD_s is sample optical density, OD_{neg} is the negative-control optical density, and OD_{pos} is the positive-control optical density. The equation does not replace method-specific haemoglobin calibration or correction for coloured extractables.

12. Evaluate complement and leucocytes

Complement activation and leucocyte response can occur without gross thrombosis. Define sampling times and stabilisation because ex vivo activation continues after collection. Consider complement fragments, leucocyte activation, platelet-leucocyte aggregates and inflammatory mediators when clinically relevant. Interpretation should preserve coupling: complement can amplify coagulation, and adherent leucocytes can change the surface presented during longer contact.

13. Account for leachables and cure residuals

Link blood testing to the exact chemical-characterisation specimen. Residual monomer, photoinitiator products, solvent and cleaning residues can affect cells or proteins without dominating bulk mechanics. ER-253 and ER-254 provide the analytical and toxicological routes; ER-257 asks whether those constituents alter blood interaction at the device surface or in the circulating phase. Extraction-only evidence does not capture surface-bound activation, while direct-contact evidence can miss a diluted systemic constituent. Both pathways may be required.

14. Treat sterilisation as a material transformation

Select sterilisation before final qualification. Recheck dimensions, conversion-sensitive chemistry, wettability, roughness, coating integrity, extractables and mechanical function after the maximum validated exposure and ageing state. Sharma, Cao, Msalleem, Kunz, Brantner, Honigmann and Thieringer measured sterilisation-associated dimensional changes in printed biocompatible resins [7]. Their surgical-guide endpoint is not haemocompatibility, but it demonstrates that sterilisation can change a photopolymer device state. Gamma, electron-beam, ethylene-oxide, peroxide-plasma and moist-heat processes can drive different reactions. Residual sterilant and packaging interactions require their own controls.

15. Use a staged evidence strategy

Start with chemistry, surface and static screening to detect gross hazards and define mechanisms. Advance to controlled dynamic testing that represents flow and exposure. Use ex vivo or in vivo evidence only where it answers unresolved device-level questions and is ethically justified. Each stage must have predefined progression rules. A favourable static result cannot cancel adverse dynamic thrombosis, and an in vivo observation cannot rescue an analytically unexplained constituent without investigation.

16. Apply non-compensatory gates

Gate	Required evidence	Blocking failure
Contact definition	Anatomical path, duration, flow and therapy	Test panel is not justified
Finished state	Complete process, ageing and sterilisation	Article is not representative
Surface	Chemistry, morphology and conditioning state	Mechanism cannot be assigned
Blood	Donor, anticoagulant, handling and baseline	Biological variability is uncontrolled
Flow	Shear, residence, stagnation and circuit control	Dynamic result is not transferable
Blood endpoints	Platelet, coagulation, haemolysis and complement logic	Haemocompatibility is incomplete
Controls	Sensitive positive, negative and comparator controls	Assay validity is unproven
Durability	Time, coating/release stability and ageing	Initial benefit may not persist

Passing one gate does not compensate for failure of another. Residual uncertainty is routed to a discriminating experiment or a documented risk decision.

17. Integrate evidence without a single score

Construct an endpoint-by-mechanism matrix linking surface state, flow region, donor, time and readout. Preserve discordant findings. A scalar haemocompatibility score can hide a severe failure in one clinically important pathway. Interpret effect size and uncertainty, not only statistical significance. Report raw distributions, donor dependence, control separation and predefined exclusions.

18. Control lifecycle changes

Reassess after changes in formulation, supplier, pigment, printer, optical dose, wash, cure, surface finishing, coating, sterilisation, packaging, shelf life, lumen geometry or intended flow. Reuse and reprocessing require separate durability evidence. Change equivalence should be demonstrated with sensitive attributes and endpoints. Similar dimensions do not prove an unchanged blood-contacting surface.

19. Minimum reporting set

Report intended use and contact classification; finished-device state; specimen representativeness; surface chemistry and morphology; blood source and handling; flow and circuit; controls; platelet, coagulation, haemolysis, complement and leucocyte results; chemical linkage; sterilisation and ageing; deviations; statistics; unresolved questions and change triggers.

20. Knowledge boundary

The ISO records define the risk-based blood-interaction framework [1-3]. The experimental studies demonstrate that printed network design, surface chemistry, flow and sterilisation can materially change relevant observables [4-7]. None establishes haemocompatibility for an unspecified resin, device geometry, sterilisation cycle or clinical blood-contact use.

21. Limitations

References [1-3] were verified against current official ISO records; references [4-7] were verified at detailed primary-record depth. Controlled standards and jurisdictional requirements govern implementation. This review does not prescribe product-specific acceptance criteria, anticoagulation, clinical management or a universal test panel.

22. Conclusions

Blood compatibility of a photopolymer device is determined by the finished surface operating in blood under flow. Defensible qualification freezes the device state, controls the blood reagent and circuit, measures complementary activation pathways, verifies sterilisation effects and preserves discordant evidence. Static screening is useful but cannot substitute for clinically representative dynamics, and no favourable endpoint can average away a material failure elsewhere.

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