

Engineering Qualification of Vat-Printed Organ-on-Chip Materials: Optical Background, Molecular Sorption, Gas Transport, Extractables and Microfluidic Fidelity

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Statement of Significance

Direct vat-photopolymerisation can simplify organ-on-chip fabrication, but the printed polymer is not a passive container. It can alter the measured biological signal through optical background, sorption of test compounds, release of residual species, oxygen transport, surface interactions and geometry-dependent microfluidic error. This review treats the chip material as part of the experimental measurement system and proposes an assay-specific qualification framework. The objective is not to identify a universally “best” resin, but to define what must be measured before a vat-printed device can be trusted for a given biological or pharmacological question.

Keywords: organ-on-chip; microphysiological systems; vat photopolymerisation; stereolithography; DLP; LCD; microfluidics; autofluorescence; molecular sorption; gas permeability; extractables; cytocompatibility; geometric fidelity; post-processing

Abstract

Vat photopolymerisation (VPP) provides a digitally direct route to microfluidic and organ-on-chip (OoC) devices with three-dimensional geometries, rapid design iteration and increasingly accessible equipment. However, the material requirements of OoC systems are substantially more demanding than geometric printability alone. A printed photopolymer may generate fluorescence background, attenuate excitation or emission light, absorb or adsorb test compounds, release residual reactive species, alter oxygen availability, change surface-mediated cell behaviour, or distort the intended channel geometry through cure broadening and trapped-resin effects. These mechanisms can bias the biological endpoint even when the device appears mechanically intact. This review synthesises primary evidence from VPP microfluidics, cell-culture devices and OoC platforms and organises the field around five qualification domains: optical background, molecular sorption and surface interactions, gas transport, extractables/cytocompatibility, and microfluidic fidelity. Recent studies demonstrate that no single material property can be used as a universal proxy for OoC suitability: post-processing can simultaneously alter conversion, transparency, cytocompatibility and mechanics; low sorption may come with different gas-transport behaviour; and high geometric resolution may require optical attenuation strategies that narrow the microscopy window. We therefore propose an assay-informed qualification sequence that starts with the intended biological readout and test compound, then validates the printed material, post-processing state, channel geometry and time-dependent exposure conditions as one coupled system. This framing distinguishes material qualification from generic biocompatibility and provides a basis for more reproducible comparison of vat-printed OoC platforms.

1. Introduction

Organ-on-chip systems combine microfluidic control with living cells, tissues or organoids to recreate selected physiological interfaces and functions. The canonical lung-on-chip demonstrated that a microengineered device can reproduce tissue–tissue interfaces, flow and cyclic mechanical strain in a way that changes biological response relative to static culture [1]. Since then, OoC platforms have expanded into vascular, hepatic, neural, intestinal, tumour and multi-organ models. Their scientific value depends not only on the biological model but also on whether the device material preserves the concentrations, optical signals, oxygen environment, mechanics and geometry assumed by the experimental design.

VPP is attractive because it converts a digital model directly into a three-dimensional polymer structure. Transparent PEGDA-based devices were already demonstrated for bio-microfluidics in 2016 [3], and custom DLP systems subsequently pushed embedded channel dimensions into the tens-of-micrometres regime [5], alongside early demonstrations of directly printed cell-laden constructs and high-density printed valves and pumps [25,26]. More recent work has extended direct photopolymer printing to transparent cell-culture devices, low-cost LCD-printed OoC arrays, neurovascular organoid chips, multi-compartment systems and gas-exchange devices [6–15]. These results establish technical feasibility. They do not, however, establish that every printable resin is suitable for every OoC assay.

This distinction matters because the material itself can become a source of measurement error. PDMS, for example, is valued for optical clarity, elastomeric behaviour and oxygen permeability, yet its absorption of hydrophobic molecules can reduce free drug concentration in a time- and molecule-dependent manner [2,16–19]. VPP materials can reduce some of these problems, but introduce others, particularly residual photochemistry, optical absorbers, conversion gradients, surface topography and negative-feature overcure. The appropriate question is therefore not whether VPP is “better than PDMS”, but which material-induced artefacts are acceptable for the specific assay and how they are measured.

The scope of this review is deliberately narrower than general reviews of VPP microfluidics or biological response [27]. It focuses on material-induced experimental bias in vat-printed OoC systems. It does not provide a product-selection table, does not infer commercial formulation composition, and does not treat a generic biocompatibility designation as proof of suitability for a specific organ model. Existing 3Dresyns WP-42 addresses microfluidic material-jetting workflows, while ER-06 treats biological response across dental and biomedical photopolymers at system level; the present review instead centres on the interaction between a vat-printed chip material and the validity of an OoC measurement.

2. The chip material as part of the measurement system

An OoC experiment has at least four coupled layers: the biological model, the fluidic architecture, the device material and the analytical readout. A material can pass a short cytotoxicity screen yet still bias the experiment by sequestering a drug, filtering a fluorescence channel or altering oxygen tension. Conversely, a material with imperfect intrinsic cell adhesion may still be acceptable when cells are physically separated from it by an extracellular-matrix gel, a membrane, a coating or a glass imaging window. Qualification must therefore be conditional on the intended contact mode and readout.

Five artefact classes are especially recurrent in vat-printed systems. Optical artefacts arise from spectral absorption, autofluorescence, scattering and surface texture. Chemical artefacts arise from absorption into the bulk, adsorption to the surface, swelling or extraction of test molecules. Biological artefacts arise from leachables, residual reactive species, surface chemistry and sterilisation history. Transport artefacts arise when oxygen, carbon dioxide, water or other species cross the wall at rates that differ from the physiological or modelled assumption. Geometric artefacts arise when the printed channel differs from the CAD channel because of cure depth, pixelation, orientation, resin drainage, post-cure or bonding.

Domain	Mechanism	Potential experimental consequence	Minimum qualification question
Optical	Autofluorescence, absorption, scattering, surface texture	False fluorescence background; wavelength-dependent loss of signal; imaging artefacts	Does the printed-and-post-processed device preserve the actual excitation/emission channels and imaging modality used?
Molecular sorption	Bulk absorption or surface adsorption of drugs, dyes, proteins or signalling molecules	Unknown free concentration, delayed release, cross-talk between exposures	Is recovery of the relevant molecule acceptable over the real residence time and surface-to-volume ratio?
Gas transport	O ₂ /CO ₂ permeation through walls or membranes	Hypoxia, hyperoxia, altered pH control or loss of imposed gradients	Is gas transport intentionally high, intentionally low or quantitatively controlled for this organ model?
Extractables / surface	Residual monomer, oligomer, photoactive species, leachables, surface energy	Cell stress, altered proliferation/differentiation, assay interference	Has the final post-processing state been tested with the actual cell type and exposure duration?
Geometry / fluidics	Overcure, trapped resin, shrinkage, roughness, bonding distortion	Changed shear stress, residence time, membrane thickness, permeability or pressure drop	Were internal dimensions and flow behaviour measured on the finished device rather than inferred from CAD?

Table 1. Material-induced artefacts that can invalidate an OoC measurement.

3. Optical background: transparency is not enough

Optical qualification is often reduced to a statement that a resin is “clear”. For OoC work this is insufficient. Bright-field imaging, phase contrast, confocal fluorescence, widefield fluorescence and plate-reader measurements probe different spectral and geometric paths. A material may look transparent to the eye while absorbing strongly below 400 nm, producing its own fluorescence under blue excitation or introducing patterned surface texture that is visible in phase contrast.

Fritschen et al. compared a commercial transparent resin and PEGDA-based systems specifically for cell culture and OoC use [6]. Their results show why the full workflow matters: resin chemistry, photoactive additives and post-treatment changed transmission, cell response and imaging quality. One commercial material remained effectively opaque below 400 nm even after post-treatment, preventing DAPI imaging while still allowing useful green-channel fluorescence. PEGDA formulations offered broader spectral transmission but differed in negative-feature resolution and surface patterning. The conclusion is not that one chemistry is intrinsically superior, but that spectral compatibility must be matched to the actual analytical channel.

Autofluorescence should therefore be measured as a wavelength-resolved background, preferably using the same excitation/emission settings, objective, optical path and device thickness used in the biological experiment. A single value at one wavelength cannot be extrapolated across GFP, FITC, DAPI, red fluorophores or label-free modalities. Accordingly, this review does not use universal fold-difference benchmarks for autofluorescence. Comparisons should report wavelength, device thickness, optical path, instrument settings, post-processing state and comparator condition.

Surface and pixel artefacts also matter. DLP can transfer periodic surface structure into the part, which may be visible in phase-contrast imaging even when fluorescence imaging remains acceptable [6]. Coatings can reduce chemical exposure but can also change refractive index, surface roughness and fluorescence background. Musgrove et al. showed that parylene-C coating protected commercial resin prints from cytotoxic leaching while maintaining useful optical qualities [9], illustrating that optical and chemical qualification should be performed after the final coating state, not on the base resin alone.

4. Molecular sorption and assay concentration

Drug and signalling-molecule concentration is a central measurement variable in pharmacological OoC studies. PDMS is known to absorb hydrophobic small molecules into its bulk, which can reduce the free concentration and create slow release during washout [16–19]. The magnitude is compound-, time-, geometry- and surface-to-volume-dependent; hydrophobicity alone does not fully predict the behaviour [17]. This is why “PDMS-free” cannot be treated as an automatic performance claim. An alternative material must be measured against the same molecule panel and experimental geometry.

VPP materials can offer substantially lower small-molecule uptake than PDMS. In the comparative DLP study by Fritschen et al., the tested printed resins exhibited small-molecule absorption far below PDMS under the reported conditions [6]. In 2025, Grindulis et al. quantified sorption and release of pharmaceutical compounds in PDMS and cyclic olefin copolymer, again showing that material choice and molecular structure jointly determine concentration error [19]. A low-binding PFPE-based 3D-printed biochip was subsequently used for dynamic spheroid culture, explicitly targeting the non-specific binding problem that limits PDMS-based pharmaceutical assays [14].

For VPP OoC qualification, “chemical resistance” and “low swelling” are not adequate substitutes for sorption data. A material may show little dimensional swelling while still adsorbing a protein or absorbing a lipophilic drug. Conversely, a coating or surface treatment that reduces sorption may modify cell attachment or optical background. At minimum, a drug-screening platform should report inlet

concentration, outlet or recovered concentration, exposure time, washout behaviour, surface-to-volume ratio, material thickness and whether cells or proteins were present during the measurement.

5. Gas transport is application-specific, not universally beneficial

PDMS gas permeability is frequently cited as a universal advantage for OoC. In reality, gas transport is a design variable. Some models require passive oxygenation through device walls; others require a stable imposed hypoxic gradient or a controlled gas–liquid interface, in which excessive wall permeability becomes a confounder. The correct requirement therefore depends on the biological model, cell density, perfusion rate, membrane thickness, medium depth and oxygen consumption rate.

A particularly direct demonstration comes from the 2024 microfluidic artificial-lung study by Fleck et al., which used a custom photopolymerisable PDMS resin in DLP to fabricate dense blood and gas microchannels separated by thin membranes and demonstrated gas-exchange function with blood [11]. The study is important because it shows that gas transport can be engineered into a vat-printed architecture rather than assumed from a generic resin label. It also illustrates that permeability, membrane thickness, channel dimensions and pressure drop must be treated together.

Other OoC experiments deliberately create oxygen gradients using composite structures that localise gas permeability [20]. These systems reinforce a key principle: oxygen availability should be measured or modelled in the finished device. Accordingly, this review does not adopt a universal minimum oxygen-permeability threshold. No universal permeability threshold can be transferred across cell type, geometry, perfusion and wall thickness without a mass-transfer model and experimental validation.

6. Extractables, residual photochemistry and long-term cell response

VPP resins cure through photo-induced network formation and may retain unreacted or partially reacted species after printing. The biological consequence depends on molecular identity, conversion, extraction, diffusion, surface area, sterilisation and exposure duration. Macdonald et al. showed that several commercial photopolymers were highly toxic in a zebrafish embryo assay, while post-print treatment could materially change the outcome [4]. Piironen et al. later demonstrated that short-term compatibility did not predict long-term cell proliferation across common SLA resins; autoclaving had a major effect on long-term survival in the materials that tolerated it [10].

Recent work makes the workflow dependence even clearer. Fritschen et al. observed that solvent extraction and extended UV exposure changed conversion, transparency and cell viability [6]. Nelson et al. used UV–visible spectroscopy to track methacrylate-related species and found that baking, soaking and UV exposure could strongly change both cytocompatibility and mechanical properties [8]. Musgrove et al. found that leaching and overcuring alone were insufficient for sensitive primary cells in the commercial resins they tested, whereas parylene-C coating reduced cytotoxic exposure and material erosion [9].

These results show that “gas-permeable”, “PDMS-free” and “biocompatible under defined conditions” are distinct descriptors and do not form a single material class. A useful OoC qualification plan should distinguish acute cytotoxicity, long-term proliferation, phenotype-specific endpoints, extractables chemistry and assay interference. Cell lines, primary cells, organoids and barrier tissues can have very different sensitivity to the same material and workflow.

7. Microfluidic fidelity: the finished channel is the relevant geometry

Microfluidic performance is governed by the realised channel, not the CAD model. Negative features are particularly demanding in VPP because light penetrating beyond the intended layer can polymerise resin inside a nominal void. Gong et al. demonstrated that resin optical formulation and printer resolution can produce channels in the tens-of-micrometres regime [5], while later process innovations such as in-situ transfer VPP were developed specifically to reduce overcure and channel clogging in transparent resins [22].

The same issue appears in current low-cost systems. Shafique et al. reported LCD printing of lateral features around the 100- μm scale, thin embedded membranes and OoC devices using a PEGDA-based ink designed for the lower irradiance and illumination inhomogeneity of LCD printers [7]. Their work is especially relevant because it couples material formulation to the actual printer optical field rather than treating “405 nm compatibility” as sufficient. In 2025, Machla et al. further showed that build orientation altered the dimensional accuracy of an SLA-manufactured oral-mucosa chip, demonstrating that geometry and fluid dynamics are process-state dependent [15].

For OoC systems, dimensional error propagates into biological conditions. A smaller-than-designed channel increases hydraulic resistance and can alter shear stress; an over-thick membrane changes diffusion distance; surface roughness changes cell adhesion and local flow; residual resin can change both chemistry and cross-section. Dimensional validation should therefore include representative positive and negative features, channel continuity, membrane thickness, pressure/leak testing and, where flow fields matter, comparison between measured geometry and the geometry used in computational fluid dynamics.

8. Hybrid and multimaterial architectures

A major advantage of treating material properties as independent qualification axes is that no single material needs to satisfy every function. Glass can provide an optical window; PDMS or another elastomer can provide a compliant gasket or gas-permeable membrane; a rigid VPP body can provide three-dimensional fluid routing; a coating can reduce leaching or sorption; and inserted commercial membranes can provide controlled porosity.

Recent literature increasingly uses this hybrid logic. Print-pause-print strategies have embedded glass, membranes and other functional components within SLA devices [23]. Meynard et al. combined a photoprinted rigid element with PDMS to obtain sealing and dimensional control in culture chambers [13], and non-swelling hydrogel chips illustrate a further materials route for avoiding hydration-induced distortion [21]. Neurovascular organoid platforms and other open-well designs use printed bodies combined with glass coverslips, gels and external perfusion components [12,24,28]. These are not compromises that weaken the VPP proposition; they are often the correct engineering response to mutually incompatible material requirements.

Study	Printed material / route	Qualification contribution	Interpretive limit
Urrios et al., 2016 [3]	PEGDA, stereolithography	Transparent bio-microfluidic devices; cell culture on printed material	Early proof of concept; not a universal resin benchmark

Study	Printed material / route	Qualification contribution	Interpretive limit
Gong et al., 2017 [5]	Custom DLP resin	Embedded microchannels down to tens of micrometres	Custom printer/resin; geometry strongly system-dependent
Fritschen et al., 2022 [6]	Commercial + PEGDA DLP resins	Transparency, cytocompatibility, sorption, microscopy, resolution, post-treatment	Three systems; results cannot be generalised to all VPP resins
Musgrove et al., 2023 [9]	Commercial clear resins + parylene C	Reduced cytotoxic leaching/erosion; coating strategy	Coating introduces its own surface/transport state
Shafique et al., 2024 [7]	PEGDA-based LCD ink	Low-cost high-resolution OoC fabrication and thin membranes	Custom ink and specific printer optical field
Fleck et al., 2024 [11]	Photopolymerisable PDMS, DLP	Gas-exchange microfluidics with thin membranes	Artificial-lung use case; not equivalent to generic cell-culture OoC
Cook et al., 2025 [12]	Commercial clear + PEGDA DLP	Multi-compartment OoC with tubing-free pump	Platform-specific biological model and workflow
Martins et al., 2025 [14]	PFPE 3D-printed chip	Low-binding drug-relevant platform for spheroids	Different chemistry and route from conventional acrylates

Table 2. Representative primary evidence relevant to material qualification of vat-printed OoC systems.

9. Different organ models impose different material constraints

The phrase “organ-on-chip material” hides major differences between use cases. A lung or artificial-lung architecture may prioritise gas exchange and compliant membranes. A liver toxicology platform may prioritise preservation of free drug concentration, oxygen delivery and long-term cell phenotype. A blood–brain barrier model may prioritise barrier integrity, membrane geometry, low background fluorescence and permeability measurement. Tumour and immune models may be especially sensitive to adsorption of proteins, cytokines and therapeutic molecules. Organoid systems may require open access for seeding and recovery rather than monolithic enclosed channels.

This diversity argues against fixed global thresholds for permeability, autofluorescence or hardness. The qualification target should instead be derived from the biological question. For example, Salmon et al. used a 3D-printed microfluidic chip to spatially coordinate vascular cells with cerebral organoids [24], while Cook et al. used a multi-compartment printed platform to study communication with lymph-node tissue [12]. The relevant performance criteria in those systems are not identical even though both are OoC platforms.

Model class	High-priority material questions	Common failure mode if ignored
Liver / metabolic	Drug sorption, oxygen availability, long-term extractables, protein adsorption	Apparent drug potency or toxicity shifted by concentration loss or hypoxia
Lung / gas-exchange	Gas permeability, membrane thickness, compliance, leak integrity	Gas transfer and mechanical stimulus differ from design assumptions
BBB / vascular barrier	Optical background, membrane geometry, adsorption, surface chemistry	False permeability readout or altered endothelial barrier phenotype
Tumour / immune	Small-molecule and protein sorption, primary-cell sensitivity, optical background	Therapeutic exposure and immune readout biased by device material
Organoid / multicompartiment	Access geometry, low leachables, surface/coating state, imaging window	Growth/migration differences caused by device rather than biology

Table 3. Example requirement priorities by OoC model.

10. An assay-informed qualification sequence

A practical qualification workflow should begin with the experimental endpoint rather than the resin datasheet. Step 1 defines the biological readout, test molecules, cell type, exposure duration, gas environment and required imaging channels. Step 2 fixes the manufacturing state: printer, wavelength, layer thickness, exposure strategy, orientation, wash, post-cure, thermal treatment, sterilisation, coating and bonding. Step 3 measures the five artefact domains on representative finished devices. Step 4 determines whether the combined error is acceptable for the intended biological inference. Step 5 repeats critical measurements after the relevant culture or ageing period, because sorption, leaching and surface state can evolve with time.

This workflow intentionally separates material qualification from biological-device approval. A material can be useful for research-grade OoC work without implying clinical-device status. Conversely, a material described as biocompatible under a particular standard or supplier protocol can still be unsuitable for an assay if it absorbs the test compound or blocks the fluorescence channel. Evidence should therefore be reported at the level of the printed, post-processed, application-specific device.

Category	Minimum information
Material state	Resin identity or chemistry class; printer/wavelength; exposure/layer settings; orientation; wash; post-cure; sterilisation; coating/bonding
Optics	Transmission spectrum or relevant wavelengths; autofluorescence under assay channels; imaging path and wall thickness
Chemical fidelity	Recovery/sorption of relevant test compounds; exposure time; surface-to-volume ratio; washout if repeated dosing
Biological response	Cell type; direct/indirect contact; duration; viability plus phenotype-relevant endpoint; control material
Gas transport	Whether gas permeability is required or suppressed; wall/membrane thickness; measured/modelled oxygen condition where relevant
Geometry / fluids	Measured internal channel dimensions, membrane thickness, leak/pressure test and flow validation on finished devices

Table 4. Minimum reporting set for a vat-printed OoC material study.

11. Implications for photopolymer design

The evidence base suggests that OoC photoresin design is a multi-objective optimisation problem. Lower aromatic content or alternative photoactive systems may improve specific optical windows but change cure kinetics. Stronger optical attenuation can improve negative-feature definition but reduce transmission. Higher network density can reduce swelling but may alter sorption, surface chemistry or diffusion. More aggressive post-cure can reduce residual reactivity while changing modulus or dimensional state. Gas-permeable silicone-rich networks can support one class of model while being unnecessary or undesirable in another.

Accordingly, “low autofluorescence”, “gas permeable”, “low binding” and “cytocompatible” should be reported as measured properties under defined conditions, not as categorical labels. The same principle applies to commercial material positioning: no product-specific composition or performance number should be inferred from a family name.

12. Research priorities and evidence gaps

The present literature remains heterogeneous in printer architecture, resin chemistry, post-processing, geometry and biological endpoint. Head-to-head studies across multiple resins under a common OoC protocol are still uncommon. Sorption studies rarely cover the same drug panel used in biological validation. Gas permeability is often discussed qualitatively rather than linked to a device-scale mass-transfer model. Optical characterisation is frequently reported as bulk transmission without assay-specific autofluorescence. Long-term primary-cell or organoid studies are much less common than short cell-line viability tests.

Three priorities would improve comparability. First, material studies should report assay-specific optical and sorption data rather than generic transparency and chemical-resistance descriptors. Second, biological studies should record the complete post-processing state because washing, thermal treatment, sterilisation and coatings materially alter the final material. Third, geometric validation should use the actual internal channel and membrane dimensions that control transport, not only nominal printer pixel size or layer height. These priorities are methodological rather than formulation-specific and can be applied to both academic and commercial systems.

3Dresyns implementation examples

The 3Dresyns microfluidic portfolio provides examples of how commercial materials can be positioned around channel fabrication constraints without treating that positioning as complete organ-on-chip qualification. The products below illustrate viscosity, compliance, rigidity and thermal design choices; assay-specific optical background, sorption, gas transport, extractables and biological response remain separate validation requirements.

Microfluidic 3Dresyn MF F-ULV1 Clear. A clear flexible microfluidic photopolymer with ultra-low viscosity, positioned for fabrication of ultra-thin microchannels. It is a relevant implementation example where resin transport and trapped-resin removal are important geometric constraints.

Microfluidic 3Dresyn MF HDT-LV1 Clear. A low-viscosity, heat-resistant microfluidic photopolymer positioned for organ-on-chip and high-precision microchannels, with a rigid mechanical profile and low-outgassing positioning in current product documentation.

Microfluidic 3Dresyn MF RLV1 Clear. A clear rigid low-viscosity microfluidic route for precision channel fabrication. Its product positioning addresses fabrication and mechanical state, not universal low autofluorescence, low molecular sorption or a defined oxygen-permeability target.

Source basis: current 3Dresyns product and Technical Data Sheet documentation, August 2026. These commercial examples are included to connect the review framework to implementation and are not substitutes for independent application-specific validation.

13. Conclusions

Vat photopolymerisation is now a credible manufacturing route for organ-on-chip systems, including low-cost LCD platforms, high-resolution DLP microfluidics, neurovascular organoid chips, multi-compartment devices and gas-exchange architectures. The main remaining materials challenge is not simply to print smaller channels. It is to ensure that the printed material does not distort the experiment it is meant to enable.

The central conclusion of this review is that OoC material suitability is assay-specific and workflow-dependent. Optical background, molecular sorption, gas transport, extractables, surface behaviour and geometric fidelity must be evaluated as a coupled qualification problem. No single property—transparency, “biocompatibility”, permeability or solvent resistance—can stand in for that system-level assessment. This framework provides a defensible boundary between generic microfluidic printability and evidence that a vat-printed device can support a specific biological inference.

Limitations

This review is an engineering synthesis rather than a preregistered systematic review or meta-analysis. Organ-on-chip studies use heterogeneous materials, post-processing routes, assays and biological models; material-induced artefacts and suitability remain assay-, geometry- and time-dependent and should not be generalised beyond the tested conditions.

Author contributions

Juan Segurola: conceptualisation, literature synthesis, engineering framework, writing and critical review.

Competing interests

The author is affiliated with 3Dresyns by Resyner Technologies S.L. The review discusses the field at a materials-engineering level and does not disclose proprietary formulation composition. Commercial materials are not treated as independently validated unless supported by the cited evidence.

Data availability

No new experimental dataset was generated for this review. All quantitative examples discussed are attributed to the cited published studies.

Company information

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