



The Pharmaceutical Association of Thailand

Under Royal Patronage

Faculty of Pharmacy, Mahidol University

White paper – September 2026

Value-Based Procurement Framework

For Tacrolimus Procurement

TABLE OF CONTENTS

บทสรุปผู้บริหาร	3
EXECUTIVE SUMMARY	6
BACKGROUND	9
METHODOLOGY	13
The Three-Phase Consensus Development Process.....	13
Phase 1: Literature Review & Regulatory Review.....	13
Phase 2: Advisory Board Meeting.....	13
Phase 3: MCDA Consensus Workshop.....	13
FRAMEWORK & RESULTS	14
TTC4 Recommendations on Tacrolimus	14
MCDA Results	15
Knock-out Criteria for Tacrolimus Scoring.....	17
The Final MCDA Tool.....	19
APPLICATION OF THE VALUE-BASED PROCUREMENT FRAMEWORK.....	31
Phase I: Preliminary Eligibility Screening	31
Phase II: Multi-Criteria Technical Scoring	33
Phase III: Value-Based Procurement Determination	33
RECOMMENDATION & IMPLEMENTATION	35
LIMITATION	37
CONCLUSION.....	39
REFERENCES	40

ยา tacrolimus เป็นยาในกลุ่ม calcineurin inhibitor หลักที่ใช้ในการรักษาต่อเนื่องหลังการปลูกถ่ายไต (kidney-transplant maintenance therapy) ในประเทศไทย อย่างไรก็ตาม เนื่องจากยา tacrolimus มีดัชนีการรักษาที่แคบ (narrow therapeutic index) และมีความแปรปรวนของระดับยาภายในผู้ป่วยรายเดียวกัน (intra-patient variability) ในระดับสูง ทำให้ความแตกต่างระหว่างผลิตภัณฑ์เพียงเล็กน้อย อาจส่งผลกระทบต่อมีนัยสำคัญทางคลินิกต่ออัตราการรอดของไตที่ปลูกถ่าย (graft survival) ได้ เมื่อผลิตภัณฑ์ยา tacrolimus ชนิดสามัญ (generic) มีให้เลือกใช้อย่างแพร่หลายมากขึ้น คณะกรรมการเภสัชกรรมและการบำบัด (Pharmacy and Therapeutics Committee) ของโรงพยาบาลจึงต้องเผชิญกับการตัดสินใจจัดซื้อที่ส่งผลโดยตรงต่อผลลัพธ์การปลูกถ่ายอวัยวะ ในขณะที่กรอบการจัดซื้อที่มีอยู่เดิมซึ่งยึดเกณฑ์ราคาการจัดซื้อเป็นหลัก ไม่ได้ถูกออกแบบมาเพื่อรองรับความเสี่ยงเฉพาะของยากลุ่มนี้ จึงทำให้เกิดช่องว่างที่สำคัญระหว่างการได้รับการขึ้นทะเบียนตามกฎระเบียบ กับระดับความมั่นใจที่แพทย์ผู้รักษาต้องการ ก่อนที่ผลิตภัณฑ์นั้นจะถูกนำไปใช้ในการรักษาของผู้ป่วยปลูกถ่ายอวัยวะ

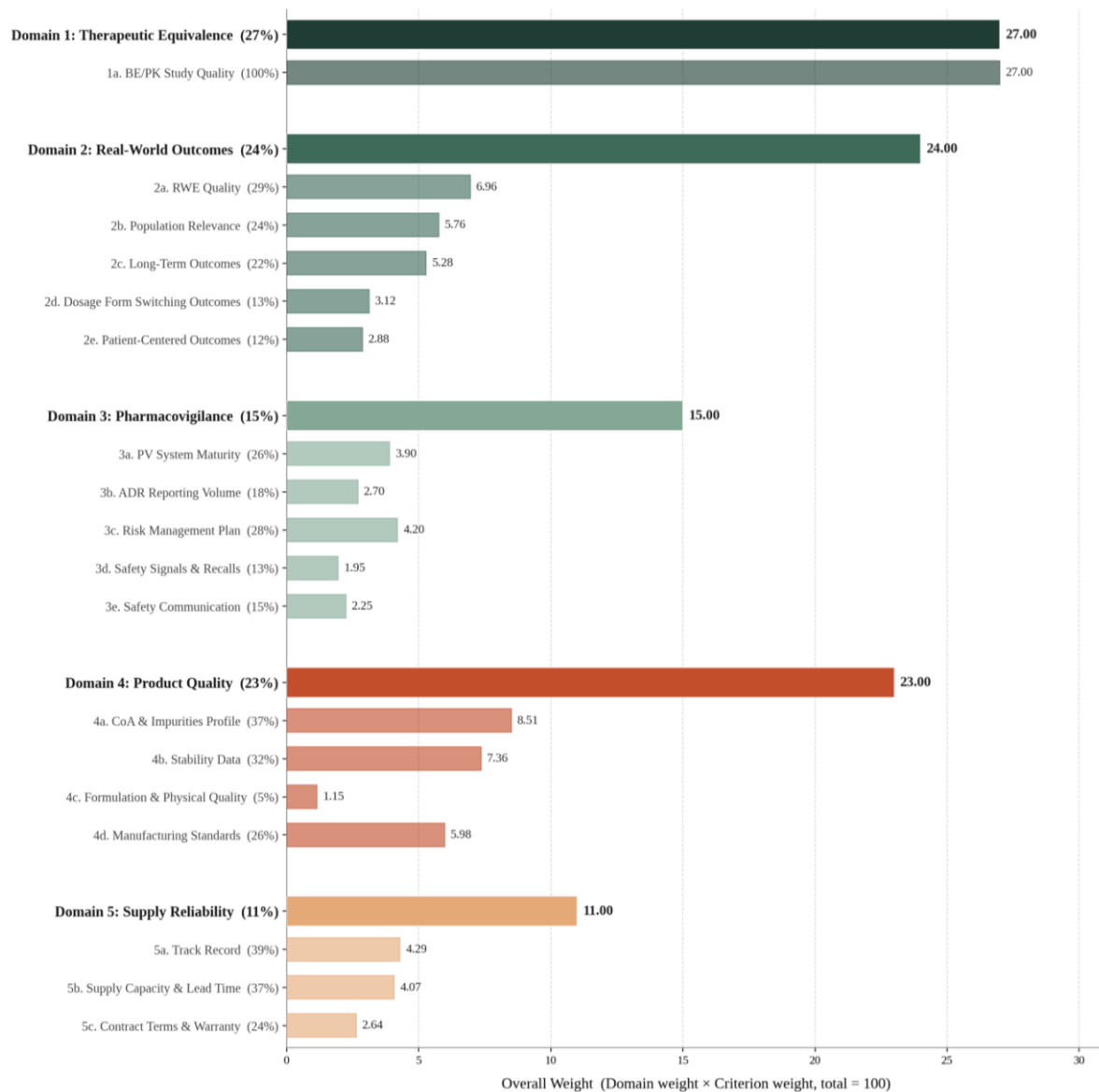
เพื่อแก้ไขปัญหาดังกล่าว จึงได้มีการดำเนินการพัฒนากรอบการจัดซื้อโดยยึดคุณค่าเป็นหลัก (Value-Based Procurement; VBP) ที่ออกแบบมาเฉพาะสำหรับยา tacrolimus โดยเริ่มต้นจากการทบทวนวรรณกรรมทางคลินิกและเอกสารที่เกี่ยวข้องอย่างเป็นระบบ ตามด้วยการประชุมคณะที่ปรึกษาซึ่งประกอบด้วยแพทย์ผู้เชี่ยวชาญด้านการปลูกถ่ายอวัยวะและเภสัชกรโรงพยาบาล เพื่อกำหนดขอบเขตของกรอบการดำเนินงาน และสุดท้ายมีการประชุมเชิงปฏิบัติการเพื่อสร้างเส้นทางของเภสัชกรโรงพยาบาลจากสถาบันต่าง ๆ ทั่วประเทศไทย โดยใช้วิธี Multi-Criteria Decision Analysis (MCDA) ตามแนวทางระเบียบวิธีของ The Professional Society for Health Economics and Outcomes Research (ISPOR) เอกสารฉบับนี้จึงนำเสนอกรอบการดำเนินงานที่ได้จากกระบวนการดังกล่าว และมีข้อเสนอแนะสำคัญดังต่อไปนี้

ข้อเสนอแนะสำคัญ:

- กำหนดให้ชีวสมมูล (bioequivalence) การปฏิบัติตามมาตรฐานการผลิต และเอกสารรายงานผลการวิเคราะห์สิ่งเจือปน เป็นเกณฑ์คัดกรองที่ไม่สามารถต่อรองได้ (non-negotiable gating requirements) แทนที่จะเป็นเพียงปัจจัยที่ให้คะแนนแบบขึ้นบันได ทั้งนี้เนื่องจากการได้รับยาต่ำหรือสูงเกินไปในยาที่มีดัชนีการรักษาแคบอาจส่งผลกระทบต่อทางคลินิกได้
- ให้ความสำคัญแก่หลักฐานเชิงประจักษ์ในการใช้จริง (real-world outcomes) และหลักฐานที่จำเพาะต่อประชากร โดยเน้นเป็นพิเศษที่ข้อมูลจำเพาะของประชากรไทยและเอเชีย เนื่องจากมีความแตกต่างในการกระจายตัวของ genotype CYP3A5 ซึ่งมีอิทธิพลต่อการปรับขนาดยา tacrolimus
- กำหนดเกณฑ์คุณภาพขั้นต่ำ (minimum-quality-threshold model) แทนอัตราส่วนประสิทธิภาพต่อราคาแบบตายตัว เพื่อให้ต้นทุนการจัดซื้อถูกนำมาพิจารณาเฉพาะในกลุ่มผลิตภัณฑ์ที่ผ่านเกณฑ์คะแนน MCDA รวมทั้งกำหนดไว้แล้วเท่านั้น โดยแนะนำควรได้คะแนนขั้นต่ำ ≥ 75 คะแนน และให้ราคาเป็นปัจจัยรองมากกว่าปัจจัยหลักในการตัดสินใจคัดเลือก
- สร้างมาตรฐานการประเมินในระดับประเทศ เพื่อทดแทนเกณฑ์การจัดซื้อที่กระจัดกระจายและขับเคลื่อนด้วยงบประมาณซึ่งใช้อยู่ในแต่ละสถาบันในปัจจุบัน โดยเริ่มต้นจากยา tacrolimus ก่อนขยายแนวทางนี้ไปยังยากดภูมิคุ้มกันชนิดอื่นต่อไป

จากฉันทามติของคณะผู้เชี่ยวชาญ เครื่องมือ MCDA ที่ได้จึงกระจายน้ำหนักการประเมินออกเป็น 5 โดเมน

โดยโครงสร้างน้ำหนักฉบับสมบูรณ์แสดงไว้ในภาพที่ 1



ภาพที่ 1: Overall weights of the five MCDA domains.

EXECUTIVE SUMMARY

Tacrolimus remains the cornerstone calcineurin inhibitor in kidney-transplant maintenance therapy in Thailand, but its narrow therapeutic index and substantial intra-patient variability mean that even modest differences between products can translate into clinically meaningful consequences for graft survival. As generic tacrolimus formulations become more widely available, hospital Pharmacy and Therapeutics Committees face procurement decisions that carry direct implications for transplant outcomes, yet existing purchasing frameworks were not designed to capture the specific risks this drug class presents. A selection process anchored primarily in acquisition cost therefore leaves a critical gap between regulatory approval and the level of assurance clinicians need before a product enters a transplant patient's regimen.

To close this gap, a structured three-phase process was undertaken to develop a Value-Based Procurement (VBP) framework tailored specifically to generic tacrolimus. The process began with a literature review of the clinical and regulatory literature, followed by an advisory board of transplant physicians and hospital pharmacists convened to define the framework's scope, and concluded with a consensus workshop in which hospital pharmacists from institutions across Thailand using Multi-Criteria Decision Analysis (MCDA) in accordance with The Professional Society for Health Economics and Outcomes Research (ISPOR) methodology. This white paper presents the resulting framework, including the following key recommendations.

Key recommendations:

- **Treat bioequivalence, manufacturing compliance, and impurity documentation as non-negotiable gating requirements** rather than graded scoring factors, given the clinical consequences of under- or over-exposure in a narrow therapeutic index drug.
- **Give meaningful consideration to real-world outcomes and population-relevant evidence**, with particular attention to Thai- and Asian-specific data given documented differences in CYP3A5 genotype distribution and their influence on tacrolimus dosing.
- **Adopt a minimum-quality-threshold model in place of a fixed performance-to-price ratio**, so that acquisition cost is considered only among products that have already cleared a defined composite MCDA score, recommended at least a 75-point threshold, keeping cost a secondary rather than primary determinant of selection.
- **Standardize this evaluation nationally**, replacing the fragmented, budget-driven criteria currently used across institutions, beginning with tacrolimus before extending the approach to other immunosuppressive agents.

Grounded in the consensus of the expert panel, the resulting MCDA tool distributes evaluation weight across five domains with the full weighting structure presented in Figure 1.

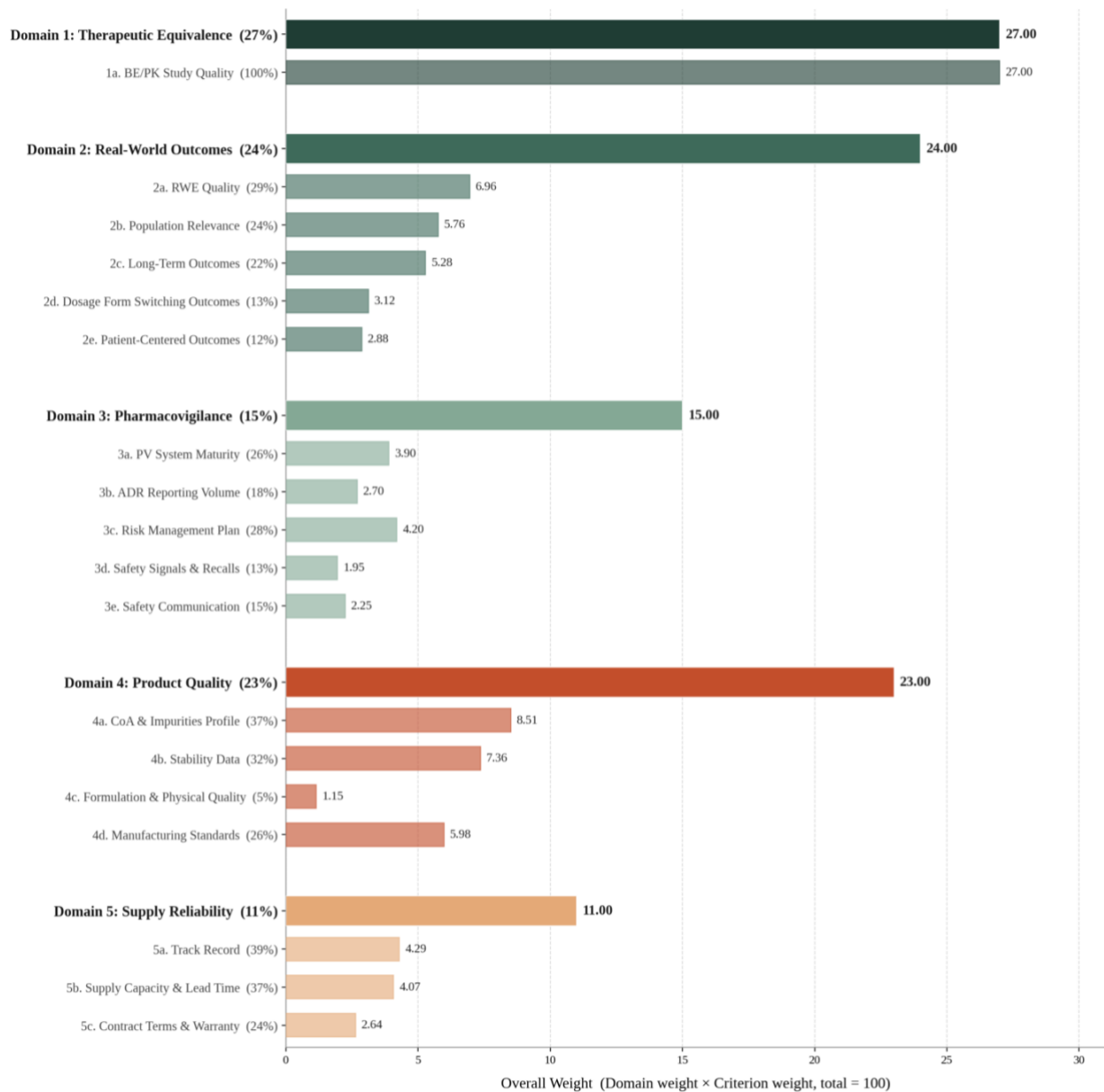


Figure 1: Overall weights of the five MCDA domains.

BACKGROUND

Kidney transplantation is the most frequently performed solid-organ transplantation in Thailand (1). Tacrolimus has become a preferred calcineurin inhibitor component of kidney-transplant maintenance therapy based on robust evidence from pivotal randomized trials. Notably, the SYMPHONY trial demonstrated that a low-dose tacrolimus-based regimen achieved superior 12-month renal function, lower biopsy-proven acute rejection, and higher graft survival compared with cyclosporine- or sirolimus-based regimens in 1,645 de novo recipients. These findings contributed substantially to the widespread adoption of tacrolimus-based maintenance regimens, although contemporary practice also reflects subsequent evidence, guidelines, toxicity considerations, and individualized risk assessment (2, 3). Consequently, the Thai Transplant Care Guideline (TTC 4, 2025) strongly recommends the triple regimen of tacrolimus, a mycophenolate preparation, and corticosteroids as the standard maintenance therapy (4).

Tacrolimus is a narrow therapeutic index (NTI) immunosuppressant for which small fluctuations in systemic exposure can lead to severe clinical consequences. Underexposure may increase the risk of acute or chronic graft rejection, whereas overexposure may cause nephrotoxicity and other dose-related adverse effects. Because tacrolimus exposure is influenced by formulation, food intake, drug interactions, organ function, adherence, and pharmacogenetic factors, routine therapeutic drug monitoring (TDM) is essential to individualize dosing (5-7).

Beyond inter-individual variability, tacrolimus exhibits substantial intra-patient variability (IPV), defined as the fluctuation of drug exposure within the same patient over time. In a multicenter cohort of more than 6,600 deceased-donor kidney-transplant recipients, approximately one-third had late tacrolimus IPV of at least 30%. Compared with patients with

IPV below 30%, graft-loss risk was 32% higher among those with IPV of 30–44% and 66% higher among those with IPV of at least 45%. These findings indicate that maintaining stable exposure, rather than merely achieving an isolated therapeutic trough concentration, is clinically important (8).

Pharmacogenetic variation further contributes to variability in tacrolimus dose requirements. Individuals carrying the functional CYP3A5*1 allele express CYP3A5 and generally clear tacrolimus more rapidly than CYP3A5*3/*3 non-expressers, often requiring higher doses to achieve comparable trough concentrations. In a Thai kidney-transplant cohort, CYP3A5 genotype was associated with tacrolimus exposure and dose requirements; patients with the CYP3A5*1/*1 genotype required higher doses during the early post-transplant period than patients with *1/*3 or *3/*3 genotypes. These findings support the importance of TDM and caution against assuming that tacrolimus exposure is uniform across patients or populations (9-11).

This complex pharmacological profile distinguishes tacrolimus from conventional oral small-molecule medications in generic substitution and procurement; a distinction already reflected in international policy. Several European countries, including the United Kingdom, Spain, Denmark, Germany, and Norway, continue to classify tacrolimus as a non-substitutable medication. Similarly, both the European Society for Organ Transplantation (ESOT) and the European Medicines Agency (EMA) recommend close therapeutic monitoring whenever patients are switched between branded and generic tacrolimus formulations (12-17). This caution is not merely theoretical. In 2023, twelve years after its initial approval, the U.S. Food and Drug Administration (FDA) revised the therapeutic equivalence rating of Accord Healthcare Inc.'s tacrolimus product from AB to BX (18).

Bioequivalent generic products can offer genuine cost savings, but selection cannot rely on acquisition price or bioequivalence study results alone; procurement must also account for strict bioequivalence standards (e.g., narrowed therapeutic equivalence margins), pharmacovigilance, local bioavailability data in Asian and Thai populations, and supply continuity, to prevent the involuntary brand switching that TTC 4 strictly discourages (4).

The clinical stakes of substitution are reflected in cost data as well. Hauch et al. (2015) found that, in the first year after transplantation, patients receiving generic tacrolimus required significantly more dose adjustments than those receiving the branded formulation (5.42 vs. 3.59 dose changes; $p = 0.038$) and experienced a higher incidence of acute rejection (23.1% vs. 10.2%; $p = 0.024$). The estimated USD 18,000 saved on drug acquisition was outweighed by the USD 652,862 in costs from managing the resulting rejection episodes, demonstrating that lower acquisition costs may not necessarily translate into overall healthcare savings once downstream clinical consequences are considered (19).

An analogous cost asymmetry is evident within the Thai context. A Thai cost-utility analysis of kidney transplantation at a major transplant center reported that the cost of a kidney transplant procedure ranges from USD 7,816 for preemptive living-related transplantation to USD 13,908 for non-preemptive deceased-donor transplantation, while ongoing hemodialysis costs an estimated USD 13,734 annually (20). Where rejection precipitates graft failure, a patient requiring re-transplantation therefore incurs not only the cost of a subsequent transplant procedure but also the cumulative cost of interim dialysis during the wait for a donor organ, a wait of approximately five years for deceased-donor transplantation in the Thai context (20, 21). Combined, these downstream costs may substantially exceed the incremental acquisition-cost savings typically realized from substituting a lower-cost generic immunosuppressant, underscoring the limitations of price-based procurement as a sole basis for selection.

Taken together, the clinical stakes of therapeutic inequivalence and the downstream costs of complications underscore the inadequacy of acquisition price as a standalone procurement criterion. Therefore, this white paper documents the development of a Value-Based Procurement (VBP) Framework specifically tailored to generic tacrolimus procurement in the Thai healthcare context. Its structural design incorporates the Most Economically Advantageous Tender (MEAT) framework and Multi-Criteria Decision Analysis (MCDA), developed through a formal consensus process among practicing hospital pharmacists from across the country, to give hospital Pharmacy and Therapeutics Committees (PTC) scientifically grounded, TTC 4-aligned criteria that safeguard long-term graft survival and patient safety over lowest-cost purchasing.

METHODOLOGY

THE THREE-PHASE CONSENSUS DEVELOPMENT PROCESS

This study employed a mixed-methods approach to ensure a comprehensive and operationally acceptable framework. The research was conducted through the following three key phases:

PHASE 1: LITERATURE REVIEW & REGULATORY REVIEW

An extensive review of existing literature, clinical practice guidelines, and regulatory documents was conducted to establish the scientific foundation and policy context for the framework.

PHASE 2: ADVISORY BOARD MEETING

An expert advisory panel, comprising transplant physicians and specialist pharmacists from 10 institutions, was convened on 30 May 2026 to critically assess the limitations of the current procurement model for immunosuppressive agents, confirm existing challenges in the Thai transplant care system, and establish the critical need for developing a Patient Value-Based Procurement framework aligned with the TTC 4 (2025) guidelines (4).

PHASE 3: MCDA CONSENSUS WORKSHOP

An expert consensus workshop, including 29 specialist hospital pharmacists from 14 institutions across Thailand, was convened on 12 July 2026. The workshop was organized to develop and ratify an MCDA-based Value-Based Procurement framework tailored to the selection of tacrolimus within Thailand's healthcare system. The workshop utilized MCDA methodology in accordance with International Society for Pharmacoeconomics and Outcomes Research (ISPOR) guidelines.

FRAMEWORK & RESULTS

TTC4 RECOMMENDATIONS ON TACROLIMUS

The Thai Transplant Care Guidelines 4 recommended a triple regimen of tacrolimus, mycophenolic acid, and corticosteroids as the standard maintenance regimen for adult kidney-transplant recipients and strongly recommended TDM of calcineurin inhibitors. Close monitoring of tacrolimus trough concentrations is mandatory during the early post-transplant phase and following any clinical changes, dose adjustments, or product substitutions. Additionally, CYP3A5 pharmacogenomic testing may be considered to guide initial dosing, particularly given the high prevalence of CYP3A5 expressers in the Thai population (4). These clinical recommendations directly impact procurement policies, because TTC 4 identifies product switching as circumstances requiring renewed TDM. Consequently, procurement decisions should look beyond acquisition price and minimum regulatory registration. Evaluating formulation consistency, rigorous bioequivalence (BE) evidence, population-specific pharmacokinetic data, supply stability, and post-marketing surveillance is critical to mitigate the clinical risks associated with tacrolimus's NTI and high IPV.

To address these challenges, the expert transplant pharmacists meeting convened to develop a consensus-driven VBP framework tailored to the Thai healthcare setting. Utilizing MCDA through iterative, anonymous voting rounds followed by structured discussions, the panel subsequently reached unanimous consensus on the framework's five-domain structural evaluation model as presented in Figure 1, Table 1, and Table 2.

MCDA RESULTS

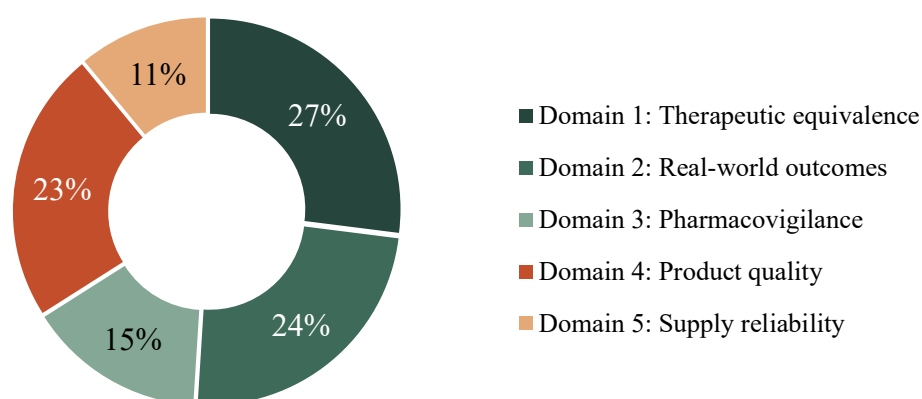


Figure 1: Overall Weights of Domains

Therapeutic equivalence (27%) and Real-world outcomes (24%) receive the two highest weights, together making up 51% of the total score. As intra-patient variability in NTI drug drives graft loss, evidence that a candidate product matches the reference product, and performs consistently in real-world Thai/Asian use, is more important than for a typical generic. Product quality is weighted third, at 23%, because tacrolimus's clinical performance is highly sensitive to manufacturing consistency: a batch-to-batch impurity or stability problem can directly cause TDM instability, which is less likely for a drug with a wider therapeutic index. Pharmacovigilance (15%) and Supply reliability (11%) receive lower weights. Both remain part of the score, but they are weighted below the three domains that most directly determine whether the drug behaves predictably in a given patient.

Table 1: Weighting and relative contribution of criteria.

Domain / Criteria	Weight within domain	Overall weight
Domain 1: Therapeutic equivalence (27%)		
1a. BE/PK study quality	100%	27.00%
Domain 2: Real-world outcomes (24%)		
2a. RWE quality	29%	6.96%
2b. Population relevance	24%	5.76%
2c. Long-term outcomes	22%	5.28%
2d. Dosage form switching outcomes	13%	3.12%
2e. Patient-centered outcomes	12%	2.88%
Domain 3: Pharmacovigilance (15%)		
3a. PV system maturity	26%	3.90%
3b. ADR reporting volume	18%	2.70%
3c. Risk management plan	28%	4.20%
3d. Safety signals and product recalls	13%	1.95%
3e. Safety communication	15%	2.25%
Domain 4: Product Quality (23%)		
4a. Certificate of Analysis & impurities profile	37%	8.51%
4b. Stability data	32%	7.36%
4c. Formulation & physical quality	5%	1.15%
4d. Manufacturing standards	26%	5.98%
Domain 5: Supply Reliability (11%)		
5a. Track record	39%	4.29%
5b. Supply capacity and lead time	37%	4.07%
5c. Contract terms and warranty	24%	2.64%

KNOCK-OUT CRITERIA FOR TACROLIMUS SCORING

During the consensus workshop, panelists agreed that certain failures in the scoring tool represent unacceptable risk and should trigger automatic exclusion (“knock-out”) rather than being treated as low scores. These criteria apply to three domains where the absence of adequate evidence or documented non-compliance cannot be offset by strong performance in other domains.

Criterion 1a

Therapeutic Equivalence:

A product is excluded from scoring if ****any**** of the following conditions are met:

- No systematic BE or PK comparability report is available.
- Only non-comparative PK data are provided, or PK data are derived from a non-comparable product.
- There is documented prior material objection from a regulatory authority regarding the product’s BE/PK profile.
- There is evidence that the product has failed to meet BE criteria in a relevant study.
- The manufacturer refuses to provide BE/PK data in a manner that prevents transparent assessment.

Criterion 4a

Certificate of Analysis & Impurities Profile:

For NTI products, the following CoA-related scenarios are designated as knock-out criteria:

- The CoA reports only “conforms/pass” without numerical impurity values, or provides only total impurities without a breakdown by individual impurity species.
- The CoA is missing key safety-relevant data, such as elemental impurities, or shows batches near specification limits or out-of-specification without adequate explanation.
- The manufacturer cannot supply a CoA for commercially distributed batches, or has a documented history of chronic impurity problems.

Criterion 4d

Manufacturing Standards:

A product is excluded from scoring if ****any**** of the following conditions apply:

- There is no valid Good Manufacturing Practice (GMP) certificate for the manufacturing site.
- The manufacturing site’s GMP certification has been revoked.
- There is documented evidence of GMP non-compliance that poses a patient safety risk.
- There is evidence that the product has failed to meet BE criteria in a relevant study.
- The manufacturer refuses to provide BE/PK data in a manner that prevents transparent assessment.

Across all three criteria, the panel emphasized that these are not situations where a lower score appropriately reflects lower quality of evidence. Instead, they represent critical evidence gaps or compliance failures that pose unacceptable risk for NTI products. Accordingly, they are treated as disqualifying conditions within the MCDA framework, distinct from the remainder of the tool, which is designed to weigh relative strengths and weaknesses across domains.

THE FINAL MCDA TOOL

The distribution of weights within the final MCDA tool (Table 2) reveals a deliberate concentration of scoring authority in a small number of high-stakes criteria. Most notably, Domain 1 (Therapeutic Equivalence) consists of a single criterion, BE/PK Study Quality, which alone carries the entire 27% domain weight and represents the highest-weighted individual criterion in the framework, exceeding even the top-weighted criterion within Product Quality (Certificate of Analysis & Impurities Profile, 8.51%) by more than threefold. This design reflects the panel's position that, for an NTI drug such as tacrolimus, no combination of favorable evidence in other domains can offset an inadequately demonstrated bioequivalence profile: a product that performs strongly on real-world outcomes, pharmacovigilance, or supply reliability cannot compensate for a marginal or absent BE/PK dataset. In effect, Criterion 1a functions as a de facto second gatekeeping mechanism alongside the formal knock-out criteria, even though it remains part of the graded scoring system rather than a strict exclusion rule.

Beyond Domain 1, the internal weighting pattern across the remaining four domains points to a consistent underlying logic: within each domain, the panel assigned the greatest internal weight to the criterion most directly tied to patient safety or graft outcome, rather than to operational or administrative considerations. RWE Quality (29%) leads Domain 2, Risk

Management Plan (28%) leads Domain 3, Certificate of Analysis & Impurities Profile (37%) leads Domain 4, and Track Record (39%) leads Domain 5. By contrast, criteria addressing softer or harder-to-verify dimensions, such as Patient-Centered Outcomes (12%) in Domain 2 and Formulation & Physical Quality (5%) in Domain 4, received comparatively modest internal weight, as such evidence is less consistently available at the time of tendering. Taken together, the weighting structure of the Final MCDA tool operationalizes the framework's stated priority of safeguarding long-term graft survival and patient safety over administrative convenience, while still preserving a defined, if modest, role for operational and commercial considerations such as supply reliability and contract terms.

Table 2: Final MCDA tool.

Domain 1: Therapeutic Equivalence — 27%		
Criterion	Tier	Evidence description
1a. BE/PK Study Quality <i>Weight 100% · Max 27</i>	100%	BE/PK study designed per FDA Product-Specific Guidance (PSG) e.g., tacrolimus, cyclosporine), consistent with ICH M13A and NTI-drug requirements. Uses an appropriate replicate crossover design (e.g., 3-period/3-sequence or 4-period/2-sequence) to assess intra-subject variability and support the tightened BE acceptance range; no concomitant medication affecting drug levels is used. Includes both fasted and fed condition studies, since food affects the drug's bioavailability. Acceptance range applied to AUC_{0–72} (reflecting tacrolimus's long half-life) and C_{max} as specified in the applicable guideline, with all key parameters passing. Sample size $n \geq 36$ (per a power analysis appropriate for NTI and/or highly variable drugs) in <i>Thai patients</i>. Includes additional assessment relevant to real-world use, such as steady-state PK or trough-level data in transplant patients switched from innovator to generic, showing no adverse effect on graft function. The BE/PK study report is complete (protocol, analytical method validation, statistical analysis) and has been certified by a regulatory authority or a credible academic journal. <i>Score: 27</i>
	75%	BE/PK study designed per FDA Product-Specific Guidance (PSG) (e.g., tacrolimus, cyclosporine), consistent with ICH M13A and NTI-drug requirements. Uses an appropriate replicate crossover design (e.g., 3-period/3-sequence or 4-period/2-sequence) to assess intra-subject variability and support the tightened BE acceptance range; no interacting concomitant medication, and both fasted and fed condition studies. Acceptance range applied to AUC and C_{max} as specified in the applicable guideline, with all key parameters passing. Sample size sufficient ($n \geq 36$) per an appropriate power analysis, in <i>Thai patients</i>. Includes additional assessment relevant to real-world use, such as steady-state PK or trough-level data in transplant patients switched from innovator to generic, showing no adverse effect on graft function. The BE/PK study report is complete (protocol, analytical method validation, statistical analysis) and has been certified by a regulatory authority or a credible academic journal. <i>Score: 20.25</i>
	50%	BE/PK study designed per FDA Product-Specific Guidance (PSG) e.g., tacrolimus, cyclosporine), consistent with ICH M13A and NTI-drug requirements. Uses an appropriate replicate crossover design (e.g., 3-period/3-sequence or 4-period/2-sequence) to assess intra-subject variability and support the tightened BE acceptance range; no concomitant medication affecting drug levels is used. Includes both fasted and fed condition studies, since food affects the drug's bioavailability.

Domain 1: Therapeutic Equivalence — 27%

Criterion	Tier	Evidence description
		Acceptance range applied to AUC and Cmax as specified in the applicable guideline, with all key parameters passing. Sample size sufficient ($n \geq 36$) per a power analysis appropriate for NTI and/or highly variable drugs, conducted in a <i>foreign population with a population structure similar to Thai patients</i>. In addition, the submission includes a supplementary BE study conducted in Thai patients or a Thai population, meeting at minimum standard of 25% tier (a full BE study per ASEAN, EMA, or Thai FDA standards (a product-specific PSG is not required), using a standard 2×2 crossover design or an appropriate replicate design per ICH M13A with a clearly stated rationale; both fasted and fed condition studies; a 90% CI of AUC and Cmax within 80.00–125.00%, supported by academic discussion of why this range is appropriate for the immunosuppressant in question; and a sample size of $n \geq 24$ with the calculation explained on statistical grounds.) Includes additional assessment relevant to real-world use, such as steady-state PK or trough-level data in transplant patients switched from innovator to generic, showing no adverse effect on graft function. The BE/PK study report is complete (protocol, analytical method validation, statistical analysis) and has been certified by a regulatory authority or a credible academic journal. <i>Score: 13.5</i>
	25%	Full BE study conducted per ASEAN, EMA, or Thai FDA standards consistent with current guidelines, without requiring a product-specific PSG. Uses a standard 2×2 crossover design, or an appropriate replicate design per ICH M13A with a clearly stated rationale; no interacting concomitant medication is used. Includes both fasted and fed condition studies. Acceptance range: 90% CI of AUC and Cmax falls within 80.00–125.00%, supported by academic discussion of why this range is appropriate for the immunosuppressant in question. Sample size $n \geq 24$ in Thai patients, with the sample-size calculation explained on statistical grounds. Complete analytical method validation (accuracy, precision, stability) per FDA Bioanalytical Method Validation guidance. Steady-state or comparative TDM data may not yet be available, but the submission is supported by a good-quality RCT/PK study. Certified by a regulatory authority or credible academic journal, with a BE study in Thai patients or population conducted in a study format different from those described above. <i>Score: 6.75</i>

Domain 2: Real-World Outcomes — 24%

Criterion	Tier	Evidence description
2a. RWE quality <i>Weight 29% · Max 6.96</i>	100%	Systematic review/meta-analysis (incl. network meta-analysis) evaluating the impact of immunosuppressant switching on graft survival, rejection, or safety, published in a high-impact journal (Lancet, BMJ, JAMA); or an IPD meta-analysis / large multi-country registry. <i>Score: 6.96</i>
	75%	≥ 2 RCTs, or a pragmatic RCT comparing innovator vs. generic, published in a Q1/Q2 transplant/immunology journal; supported by a large observational cohort/registry. <i>Score: 5.22</i>
	50%	A single RCT, or a moderate-sized cohort study/registry (hundreds of patients), using basic statistical methods (Kaplan–Meier, Cox regression); overall evidence indicates the generic is non-inferior. <i>Score: 3.48</i>
	25%	Only a small prospective cohort or single-center registry, without a clear comparison to the innovator. <i>Score: 1.74</i>
	0%	No RCT, cohort, registry, or systematic review addressing graft survival or long-term safety. <i>No score awarded.</i>
2b. Population relevance <i>Weight 24% · Max 5.76</i>	100%	Data from a Thai transplant registry or a Southeast Asian cohort with similar population structure and TDM access. <i>Score: 5.76</i>
	75%	Data from other Asian countries (Japan, China, South Korea, Taiwan, Singapore) using a similar immunosuppressant regimen. <i>Score: 4.32</i>
	50%	Evidence mostly from the US/EU, with a reasonable rationale for extrapolating to Thai/Asian patients. <i>Score: 2.88</i>
	25%	Data from a substantially different population (e.g., pediatric-only data when the hospital uses it in adults, or a different indication). <i>Score: 1.44</i>
	0%	No clinical evidence that can reasonably be extrapolated to the hospital's patient population. <i>No score awarded.</i>
2c. Long-term outcomes <i>Weight 22% · Max 5.28</i>	100%	Outcomes (graft survival, patient survival, chronic rejection, malignancy) followed ≥ 60 months; uses survival analysis and reports hazard ratio/relative risk; kidney graft survival rate ≥ 80%. <i>Score: 5.28</i>
	50%	Outcomes (graft survival, patient survival, chronic rejection, malignancy) followed ≥ 12 months; with a kidney graft survival rate of ≥ 90%, and post-transplant patient survival rates ≥ 70% for liver transplantation and ≥ 40% for heart transplantation, respectively. <i>Score: 2.64</i>

	0%	No real-world clinical outcome follow-up data. <i>No score awarded.</i>
2d. Dosage form switching outcomes <i>Weight 13% · Max 3.12</i>	100%	≥ 12-month outcome data (graft survival, patient survival, chronic rejection, malignancy) confirming interchangeability when switching between capsule and prolonged-release capsule formulations of tacrolimus available in Thailand. <i>Score: 3.12</i>
	50%	PK-based interchangeability data confirming switching among IV, capsule, and prolonged-release capsule formulations available in Thailand. <i>Score: 1.56</i>
	0%	No switching-study data found. <i>No score awarded</i>
2e. Patient-centered outcomes <i>Weight 12% · Max 2.88</i>	100%	PRO measured with a validated instrument (SF-36, EQ-5D, kidney-transplant-specific QoL scale or equivalent tools); adherence quantified (MPR, PDC). <i>Score: 2.88</i>
	75%	QoL/satisfaction assessed with a structured questionnaire, even if not an internationally validated tool. <i>Score: 2.16</i>
	50%	Indirect adherence data (prescription refill, clinic attendance) without quantitative measurement. <i>Score: 1.44</i>
	25%	Only a statement that the patient "tolerated the drug well," with no defined measurement method. <i>Score: 0.72</i>
	0%	No PRO, QoL, or adherence data for the product. <i>No score awarded.</i>

Domain 3: Pharmacovigilance — 15%

Criterion	Tier	Evidence description
3a. PV system maturity <i>Weight 26% · Max 3.9</i>	100%	Complete PSMF per EU GVP Module I–II and Thai FDA requirements; formally appointed QPPV; PV system covers both active and passive surveillance for immunosuppressant-specific signals; PSUR/PBRER submitted on time; PV QA audits and CAPA in place. <i>Score: 3.9</i>
	75%	PSMF covers the core structure, but some documentation is incomplete; QPPV is functioning but signal assessment is more reactive than proactive. <i>Score: 3.93</i>
	50%	Basic PV system and responsible personnel in place, but no full PSMF; no plan for immunosuppressant-specific signals. <i>Score: 1.95</i>
	25%	Only a PV framework/SOP outline that hasn't been updated; ADR reporting is ad hoc. <i>Score: 0.98</i>
	0%	No evidence of a PV system, PSMF, or PV personnel; no structure to support ADR reporting. <i>No score awarded.</i>
3b. ADR reporting volume <i>Weight 18% · Max 2.7</i>	100%	>100 reports/year (relative to market share); consistently submitted to HPVC/FAERS/VigiBase; systematic disproportionality analysis (ROR) and signal detection. <i>Score: 2.7</i>
	75%	~50–100 reports/year, submitted consistently with appropriate follow-up. <i>Score: 2.03</i>
	50%	~10–50 reports/year or inconsistent reporting; mainly passive spontaneous reporting. <i>Score: 1.35</i>
	25%	<10 reports/year despite reasonable market share; lacking qualitative detail. <i>Score: 0.68</i>
	0%	No ADR reports in major databases despite real-world use. <i>No score awarded.</i>
3c. Risk management plan <i>Weight 28% · Max 4.2</i>	100%	RMP per EMA GVP Module V/Thai FDA; complete safety specification (identified risks, potential risks, missing information); PASS, registry, or long-term follow-up for infection, malignancy, nephrotoxicity; specific RMMs (educational materials, monitoring recommendations). <i>Score: 4.2</i>
	75%	RMP clearly identifies major risks and a safety-monitoring strategy; routine + additional RMMs. <i>Score: 3.25</i>
	50%	RMP identifies risks but has no further study plan or immunosuppressant-specific RMMs. <i>Score: 2.1</i>

	25%	RMP contains only partial information and is not updated with new data. <i>Score: 1.05</i>
	0%	No RMP, or the RMP is inaccessible. <i>No score awarded.</i>
3d. Safety signals and product recalls <i>Weight 13% · Max 1.95</i>	100%	No recall in the past 3 years; no serious quality-related safety signal. <i>Score: 1.95</i>
	75%	Only Class III recall(s) (labeling/packaging issues not affecting drug quality); no Class I/II recall. <i>Score: 1.46</i>
	50%	≥ 1 Class II recall, subsequently resolved. <i>Score: 0.98</i>
	25%	≥ 1 Class I recall (e.g., microbial contamination, strength mix-up). <i>Score: 0.49</i>
	0%	Multiple recalls or unresolved chronic quality signals; evidence linking quality issues to patient SAEs. <i>No score awarded.</i>
3e. Safety communication <i>Weight 15% · Max 2.25</i>	100%	DHPC/safety letters issued immediately upon new signals; labeling updated promptly in line with the latest data. <i>Score: 2.25</i>
	75%	Responds to regulatory-authority directives quickly and completely. <i>Score: 1.69</i>
	50%	Communicates only when requested or in severe cases. <i>Score: 1.13</i>
	25%	Slow or incomplete response. <i>Score: 0.56</i>
	0%	Slow or incomplete response. <i>No score awarded.</i>

Domain 4: Product Quality — 23%

Criterion	Tier	Evidence description
4a. Certificate of Analysis (CoA) & Impurities profile <i>Weight 37% · Max 8.51</i>	100%	CoA reports numerical values for all specified impurities — organic, inorganic, residual solvents, and elemental impurities — per ICH Q3A/B/C/D; BRT/BDL clearly reported; does not rely on "conforms" alone; includes immunosuppressant-specific degradation-product data; ≥ 3 recent batches consistently within specification. <i>Score: 8.51</i>
	75%	Numerical values reported for major specified impurities (top 3–5); key impurities controlled per ICH; representative CoAs across multiple batches. <i>Score: 6.38</i>
4b. Stability data <i>Weight 32% · Max 7.36</i>	100%	Long-term stability ≥ 36 months in Zone IVb (30°C/75% RH), ongoing; accelerated stability (40°C/75% RH) ≥ 6 months; photostability per ICH Q1B (Option 1 or 2); in-use stability for relevant dosage forms; documentation consistent with the labeled shelf-life. <i>Score: 7.36</i>
	75%	Long-term stability 24–36 months in Zone IVb (or at least 30°C/65–75% RH); accelerated stability complete per ICH; in-use stability may not cover all conditions. <i>Score: 5.52</i>
	50%	Long-term stability <24 months covering the requested shelf-life; accelerated data meets only the 6-month minimum; no photostability or additional in-use stability. <i>Score: 3.68</i>
	25%	Only accelerated stability (6 months) without 12 months of long-term data; or long-term studies still ongoing. <i>Score: 1.84</i>
	0%	Cannot provide a stability report per ICH Q1A/Q1B; or evidence of degradation under Zone IVb conditions without corrective measures. <i>No score awarded.</i>
4c. Formulation and physical quality <i>Weight 5% · Max 1.15</i>	100%	Consistent tablet/capsule size, shape, color, and surface texture; no capping, chipping, or cracking; clear scoring line; smooth film coat; packaging protects against moisture/light; child-resistant packaging where appropriate. <i>Score: 1.15</i>
	75%	Generally good tablet quality; minor coating imperfections that don't affect dose/stability; standard packaging. <i>Score: 0.86</i>
	50%	Acceptable physical characteristics with some limitations (e.g., slight color inconsistency, large tablet size affecting swallowability). <i>Score: 0.58</i>
	25%	Capping, chipping, rough edges, or batch-to-batch color variation observed. <i>Score: 0.29</i>

0%	Serious problems (e.g., disintegration failure, out-of-spec dissolution); complaints from multiple hospitals leading to discontinued use or cannot be evaluated. <i>No score awarded.</i>
----	---

4d. Manufacturing standards <i>Weight 26% · Max 5.98</i>	100%	Manufacturing site holds PIC/S GMP certification and has passed inspection by US FDA, EMA, and/or PMDA without major observations; WHO Prequalification where applicable; no history of GMP revocation. <i>Score: 5.98</i>
	75%	GMP certified by Thai FDA and/or under ASEAN GMP; good inspection history with no repeat major observations. <i>Score: 4.49</i>
	50%	Minimum domestic GMP certification only; not yet inspected by an international authority; may have had minor observations. <i>Score: 2.99</i>
	25%	History of major GMP observations (aseptic control, cross-contamination, data integrity), since remediated, but the history reflects ongoing risk. <i>Score: 1.5</i>

Domain 5: Supply Reliability — 11%

Criterion	Tier	Evidence description
5a. Track record <i>Weight 39% · Max 4.29</i> <i>(If the business has been operating for less than 2 years, a track record is not required.</i> <i>This assessment evaluates the overall performance of the entire company.)</i>	100%	No national/regional drug shortage or supply disruption in ≥ 3 years; no recall affecting drug availability; manufacturer has a strong reliability track record. <i>Score: 4.29</i>
	75%	Minor shortage/delay (≤1 event/year), resolved quickly with advance communication; no impact on treatment continuity. <i>Score: 3.22</i>
	50%	>1 supply issue in 3 years (2–3 events) requiring lot/pack changes or delayed delivery; mostly resolved, but the hospital should frequently manage its own buffer stock. <i>Score: 2.15</i>
	25%	Major supply issues or frequent shortages affecting treatment, requiring regimen changes or frequent brand switching. <i>Score: 1.07</i>
	0%	Chronic supply failure; cannot guarantee consistent supply. <i>No score awarded.</i>
5b. Supply capacity and lead time <i>Weight 37% · Max 4.07</i> <i>(Tailor the lead time to the specific context of each hospital)</i>	100%	MOQ aligned with the hospital's actual usage; lead time <30 days; factory capacity and buffer stock can absorb a 20–30% demand increase. <i>Score: 4.07</i>
	75%	Lead time 30–60 days, but consistently on-time delivery; good stock/logistics management. <i>Score: 3.05</i>
	50%	Lead time 60–90 days requiring significant advance planning; MOQ must be negotiated down. <i>Score: 2.04</i>
	25%	Cannot confirm continuous volume; lead time >90 days or frequently changes without notice. <i>Score: 1.02</i>
	0%	Manufacturer states it cannot supply the required volume or will discontinue the product. <i>No score awarded.</i>
5c. Contract terms and warranty <i>Weight 24% · Max 2.64</i>	100%	Full warranty covering replacement/return for any defect; clear penalty clause for late delivery; policy for returning/destroying near-expiry product with compensation. <i>Score: 2.64</i>
	75%	Basic warranty provided but no clear penalty clause; standard contract terms. <i>Score: 1.98</i>

0%

Contract terms don't emphasize compensation/accountability for late delivery; no penalty clause.
No clear quality guarantee; no compensation provision for incomplete delivery.
Contract terms place nearly all risk on the hospital (no warranty, no return, no penalty); may conflict with institutional procurement regulations. *No score awarded.*

APPLICATION OF THE VALUE-BASED PROCUREMENT FRAMEWORK

Operationalization of the ratified MCDA tool necessitates a defined evaluation sequence through which hospital PTC may translate the consensus framework into a reproducible procurement decision. The decision could be achieved through three sequential phases: a preliminary eligibility screening, a structured multi-criteria technical scoring exercise, and a final value-based determination in which acquisition cost is considered only among products that have already satisfied a defined quality standard.

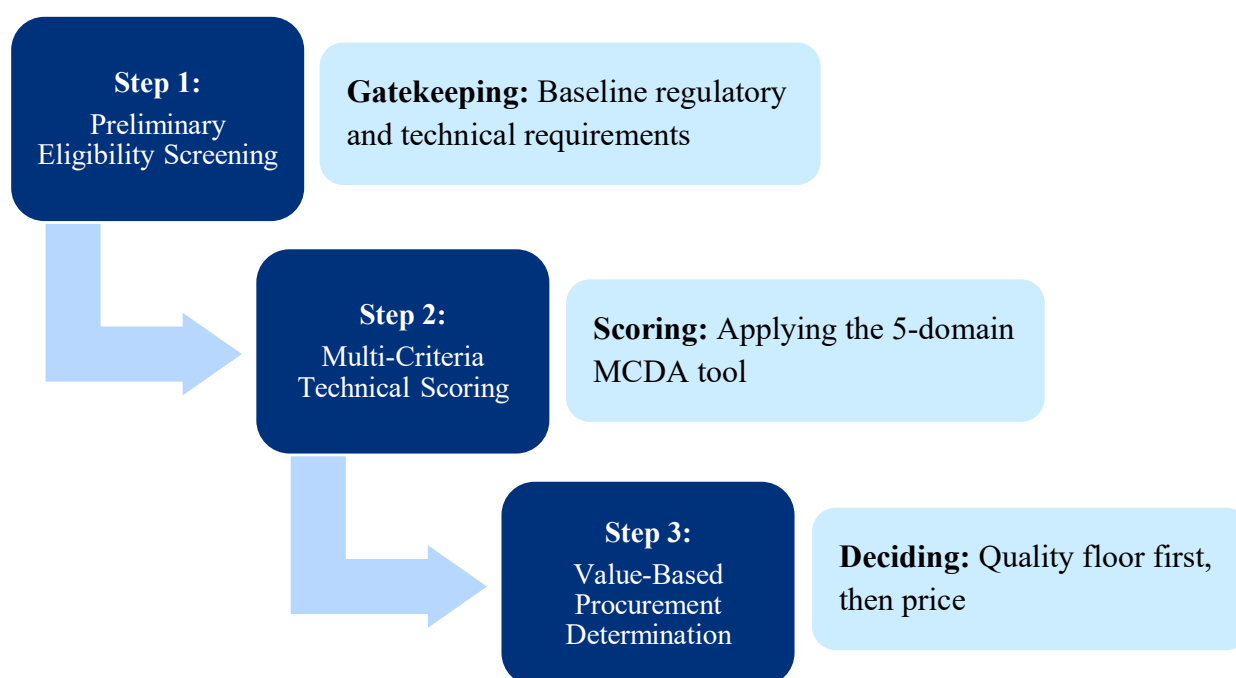


Figure 2: Decision pathway for hospital implementation.

PHASE I: PRELIMINARY ELIGIBILITY SCREENING

Before the application of the scoring instrument, candidate products are subject to a preliminary screening intended to exclude submissions that fail to satisfy fundamental regulatory and technical prerequisites. The following were identified by the consensus panel as prerequisite, rather than scored, requirements:

- **Regulatory registration and manufacturing compliance:** Products must hold current Thai FDA registration, and the manufacturing site(s) responsible for both the active pharmaceutical ingredient and the finished dosage form must hold valid GMP certification. In view of the narrow margin between sub-therapeutic exposure and toxicity characteristic of tacrolimus, the panel recommended that GMP compliance be applied as an absolute, rather than graded, criterion.
- **Bioequivalence for NTI drugs:** Conventional bioequivalence data is considered insufficient given tacrolimus's NTI. Submissions are required to demonstrate bioequivalence to the reference product using an adequately powered crossover or replicate-design study; the specific acceptance criteria are detailed under Criterion 1a in Table 2. Consistent with the Therapeutic Equivalence knock-out criterion (1a), a product is excluded at this stage if no systematic BE or PK comparability report is available; if only non-comparative PK data are provided, or the data are derived from a non-comparable product; if there is documented prior material objection from a regulatory authority regarding the product's BE/PK profile; if the product has failed to meet BE criteria in a relevant study; or if the manufacturer declines to provide BE/PK data in a manner that permits transparent assessment.
- **Current regulatory approval status:** Only currently registered, approved formulations are eligible for evaluation; products lacking adequate comparability documentation are deferred pending submission of further evidence.

Products failing to satisfy any of the foregoing criteria are excluded prior to technical scoring.

PHASE II: MULTI-CRITERIA TECHNICAL SCORING

Products satisfying Phase I proceed to evaluation against the five domains and associated weights ratified: Therapeutic Equivalence (27%), Real-World Outcomes (24%), Product Quality (23%), Pharmacovigilance System (15%), and Supply Reliability (11%). Within each domain, individual criteria are assessed against predefined evidence tiers, generally ranging from 100% to 0%, with the Committee assigning the tier corresponding to the evidence submitted. Two methodological refinements were incorporated at the panel's recommendation: first, the lowest tiers of the Certificate of Analysis and Impurities Profile criterion were redesignated as a “Do Not Consider” outcome, reflecting the panel's position that failure to meet baseline specification constitutes disqualifying, rather than merely inferior, evidence; second, the Track Record criterion under Supply Reliability was waived for manufacturers or products with fewer than two years of market presence, so as not to systematically disadvantage new market entrants. Each criterion's score is derived by multiplying its maximum weight by the achieved tier percentage; the sum of criterion scores across all five domains yields a composite MCDA score expressed out of 100.

PHASE III: VALUE-BASED PROCUREMENT DETERMINATION

Rather than applying a fixed performance-to-price ratio, the panel recommended a minimum-quality-threshold approach, whereby acquisition cost is weighed only among products that have already satisfied a defined quality floor:

- A composite MCDA score below 75 out of 100 is recommended as disqualifying, irrespective of acquisition cost, given the clinical consequences associated with graft loss and severe adverse events.

- Among products meeting the applicable threshold, hospitals may derive a value metric, such as a Cost-per-Quality-Point ratio (annual acquisition cost divided by MCDA score), to inform final selection on the basis of overall value rather than acquisition price alone.

This sequential model ensures that acquisition cost functions as a secondary determinant, applied only after therapeutic equivalence, real-world outcomes, product quality, pharmacovigilance maturity, and supply reliability have each been independently verified against a defined evidentiary standard.

RECOMMENDATION & IMPLEMENTATION

Translating the ratified framework into standard national practice requires attention to procurement policy, institutional governance, and the practical mechanisms that sustain the framework once adopted. The following recommendations address these dimensions.

Procurement Strategy and Standardization

Hospital procurement criteria for immunosuppressive agents are currently fragmented, with performance-to-price weighting ranging from 10% to 20% across institutions, largely driven by budgetary pressure rather than clinical judgment. Hospitals should adopt the ratified MCDA tool and its minimum-quality-threshold model as a shared reference standard in place of these independently set specifications.

Tacrolimus is the framework's starting point given its narrow therapeutic index and high IPV; extension to other immunosuppressants (e.g., mycophenolate mofetil, mTOR inhibitors, cyclosporine) should follow only once drug-specific criteria are developed for each, rather than applying a single template across drug classes. Criteria should also apply uniformly across all indications for which tacrolimus is stocked, not transplantation alone, to prevent unproven generics from entering the formulary through a non-transplant indication and bypassing transplant-specific safeguards.

Financial Constraints and Value Communication

Rather than treating cost containment and patient safety as competing priorities, hospitals should pair MCDA scores with a total-cost-of-care estimate, factoring in therapeutic drug monitoring burden, switching risk, and downstream costs of rejection or toxicity. This gives pharmacists a concrete, executive-facing case for value-based selection. Hospitals should also discontinue introducing unproven generics into stable patients and using a subsequent

rejection as the signal to reverse course; the framework is intended to replace this reactive approach with a proactive evidentiary gate.

Sustaining the Framework

A defined review cadence (e.g., every two to three years, or triggered by a material safety signal) should keep the framework current as evidence accumulates. A documented, auditable exception pathway should allow hospitals to manage genuine supply disruptions without informally abandoning the standard. A centrally maintained repository of manufacturer submissions and scores would reduce duplicated review effort across hospitals, and a mechanism to track post-adoption outcomes (graft survival, rejection rates, IPV) by product should feed back into periodic review, so the framework continues to incentivize manufacturers to invest in evidence rather than compete on price alone.

LIMITATION

While this framework provides a structured, evidence-based approach to generic tacrolimus procurement, several limitations should guide its application and future refinement. First, the criteria and weights presented reflect the clinical priorities and institutional experiences of the specific expert panels convened across two meetings: an advisory session with transplant physicians and hospital pharmacists from 10 institutions, and a consensus workshop with 29 hospital pharmacists from 14 institutions. A panel with a different composition, such as one drawn more heavily from non-transplant or general hospitals, might reasonably weight the five domains differently.

Second, consensus was not uniformly strong across all 18 criteria, even though the five-domain structure itself achieved unanimous agreement. Two criteria illustrate this most clearly. For Criterion 4c (Formulation and Physical Quality), panelists noted that hospitals frequently do not receive physical product samples prior to tender awards, making baseline batch-to-batch physical assessment unfeasible without prior purchasing history. This criterion is nonetheless intentionally retained in the framework to serve as an aspirational benchmark: by maintaining this standard, the framework signals the importance of physical quality to manufacturers. In practice, if no participating manufacturer is able to provide physical samples or sufficient verifiable evidence during the bidding phase, all candidate products receive an equal baseline score (e.g., 0%) for this specific criterion, ensuring a level playing field where no supplier is unfairly disadvantaged, while still upholding the institutions' uncompromising stance on quality.

For Criterion 1a (BE/PK Study Quality), the evidence tiers were substantially revised after the workshop, expanding from three tiers to the five-tier structure, in response to panelists' concern that the original structure could not adequately distinguish between BE/PK

submissions of differing quality. This revision addresses the structural gap identified during the workshop, but the revised version has not itself been confirmed by a further panel vote.

Third, several domains rely materially on data that only manufacturers can supply, which may not yet exist in the Thai market. Post-authorization outcomes (Domain 2), pharmacovigilance history (Domain 3), and Certificate of Analysis detail (Domain 4a) can only be scored to the extent a manufacturer discloses them during tendering; a manufacturer's non-disclosure and a genuine absence of underlying data are not always distinguishable from a hospital's vantage point. Most notably, Thai-population evidence for generic tacrolimus may therefore not be assessable against the framework's own highest evidentiary tier, at least until locally conducted study designs meet these recommended standards.

Finally, because generic tacrolimus products meeting these criteria have not yet been widely evaluated through actual hospital procurement in Thailand, this framework has not been empirically validated against real-world procurement outcomes. The framework should accordingly be treated as a provisional baseline model; future work should assess its feasibility, discriminatory power, and long-term impact on procurement decisions and patient outcomes as generic tacrolimus products enter the Thai market and are evaluated under it.

CONCLUSION

This white paper presents the first nationally coordinated, consensus-based VBP framework for generic tacrolimus in Thailand, developed through a structured, three-phase process engaging transplant physicians and specialist hospital pharmacists from across the country. By grounding procurement decisions in an MCDA tool that weighs therapeutic equivalence, real-world outcomes, product quality, pharmacovigilance maturity, and supply reliability, rather than acquisition price alone, the framework directly operationalizes the cautions raised in the Thai Transplant Care 4 (2025) guideline regarding unsupported product switching in a narrow therapeutic index drug.

The framework is intended as a practical, adoptable tool for hospital PTC: its minimum-quality-threshold model preserves space for responsible cost management while ensuring that no product enters a transplant patient's regimen without first clearing an evidentiary bar appropriate to the clinical stakes involved. As outlined in the accompanying recommendations, sustaining the framework's relevance will require periodic review, national-level standardization, and mechanisms to track real-world outcomes as adoption proceeds. Ultimately, this framework represents a shared commitment among Thailand's transplant pharmacy community to place long-term graft survival and patient safety at the center of procurement decisions.

REFERENCES

1. Ingsathit A, Avihingsanon Y, Rattanasiri S, Premasathian N, Pongskul C, Jittikanont S, et al. Different Etiologies of Graft Loss and Death in Asian Kidney Transplant Recipients: A Report From Thai Transplant Registry. *Transplantation Proceedings*. 2010;42(10):4014-6.
2. Ekberg H, Tedesco-Silva H, Demirbas A, Vitko S, Nashan B, Gürkan A, et al. Reduced exposure to calcineurin inhibitors in renal transplantation. *N Engl J Med*. 2007;357(25):2562-75.
3. Ekberg H, Mamelok RD, Pearson TC, Vincenti F, Tedesco-Silva H, Daloze P. The challenge of achieving target drug concentrations in clinical trials: experience from the Symphony study. *Transplantation*. 2009;87(9):1360-6.
4. Thai Transplantation Society. THAI TRANSPLANT CARE 2025 (TTC 4): Practice Guidelines on Immunosuppressive Therapy and Infectious Disease Management in Solid Organ Transplantation 2025 [Available from: https://www2.rcpt.org/web/media/content/file/2025/10/CF-1107-THAI_TRANSPLANT_CARE_2025_final-251016133648A5tyxQ.pdf].
5. Mohammadpour N, Elyasi S, Vahdati N, Mohammadpour AH, Shamsara J. A review on therapeutic drug monitoring of immunosuppressant drugs. *Iran J Basic Med Sci*. 2011;14(6):485-98.
6. Andrews LM, Li Y, De Winter BCM, Shi YY, Baan CC, Van Gelder T, et al. Pharmacokinetic considerations related to therapeutic drug monitoring of tacrolimus in kidney transplant patients. *Expert Opin Drug Metab Toxicol*. 2017;13(12):1225-36.
7. van Gelder T, Gelinck A, Meziyerh S, de Vries APJ, Moes D. Therapeutic drug monitoring of tacrolimus after kidney transplantation: trough concentration or area under curve-based monitoring? *Br J Clin Pharmacol*. 2025;91(6):1600-6.
8. Süsal C, Döhler B. Late intra-patient tacrolimus trough level variability as a major problem in kidney transplantation: A Collaborative Transplant Study Report. *Am J Transplant*. 2019;19(10):2805-13.
9. Nair SS, Sarasamma S, Gracious N, George J, Anish TS, Radhakrishnan R. Polymorphism of the CYP3A5 gene and its effect on tacrolimus blood level. *Exp Clin Transplant*. 2015;13 Suppl 1:197-200.
10. Mendoza Rojas A, Hesselink DA, van Besouw NM, Dieterich M, de Kuiper R, Baan CC, et al. High Tacrolimus Inpatient Variability and Subtherapeutic Immunosuppression are Associated With Adverse Kidney Transplant Outcomes. *Ther Drug Monit*. 2022;44(3):369-76.
11. Vannaprasaht S, Reungjui S, Supanya D, Sirivongs D, Pongskul C, Avihingsanon Y, et al. Personalized tacrolimus doses determined by CYP3A5 genotype for induction and maintenance phases of kidney transplantation. *Clin Ther*. 2013;35(11):1762-9.
12. Gemeinsamer Bundesausschuss. Benefit Assessment of Medicinal Products [14 Jul 2023]. Available from: <https://www.g-ba.de/english/benefitassessment/>.

13. Lægemiddelstyrelsen. Danish Medicine Agency [14 Jul 2023]. Available from: <https://laegemiddelstyrelsen.dk/en/>.
14. European Medicines Agency. Investigation of bioequivalence - Scientific guideline [14 Jul 2023]. Available from: <https://www.ema.europa.eu/en/investigation-bioequivalence-scientific-guideline>.
15. Ministerio de Sanidad. Ministerio de Sanidad y politica, [14 Jul 2023]. Available from: <https://www.sanidad.gob.es/home.htm>.
16. National Institute for Health and Care Excellence. NICE British National Formulary [14 Jul 2023]. Available from: <https://bnf.nice.org.uk>.
17. van Gelder T. European Society for Organ Transplantation Advisory Committee recommendations on generic substitution of immunosuppressive drugs. *Transpl Int*. 2011;24(12):1135-41.
18. United States Food and Drug Administration. FDA is changing the therapeutic equivalence rating for Accord Healthcare Inc.'s generics of Prograf (tacrolimus) oral capsules. 2023 [Available from: <https://www.fda.gov/drugs/drug-alerts-and-statements/fda-changing-therapeutic-equivalence-rating-accord-healthcare-incs-generics-prograf-tacrolimus-oral>].
19. Hauch A, John M, Smith A, Dortonne I, Patel U, Kandil E, et al. Generics: are all immunosuppression agents created equally? *Surgery*. 2015;158(4):1049-54; discussion 54-5.
20. Phongphithakchai A, Phisalprapa P, Kositamongkol C, Premasathian N, Larpparisuth N, Skulratanasak P, et al. Preemptive Living-Related Kidney Transplantation Is a Cost-Saving Strategy Compared With Post-dialysis Kidney Transplantation in Thailand. *Front Med (Lausanne)*. 2022;9:869535.
21. Thai Transplantation Society. รายงานข้อมูลการปลูกถ่ายอวัยวะประจำปี พ.ศ. 2567. 2024.



Photo 1: Participants of the MCDA consensus workshop for the Value-Based Procurement framework for generic tacrolimus, held on 12 July 2026.

Ethical Statement:

This work was funded by Astellas Pharma (Thailand); the funder had no role in the design, conduct, analysis, or interpretation of the consensus process, nor in the decision to develop or publish this white paper.