

Online Resource 2

English translation of the invitation letter and questionnaire

Article title: Manufacturer-Perceived Development and Market-Entry Risks Associated with Discontinuation and Non-Launch of Generic Medicines in Japan: A Cross-Sectional Survey of Marketing Authorization Holders

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***Note.** This document is an English translation of the invitation letter and web-based questionnaire used in the survey. The survey was administered in Japanese. Response options and rating scales are reproduced as presented to respondents. The questionnaire covered broader topics than the present article. The analyses reported in this article used Q1–Q4, Q6–Q7, and Q9; the other items are provided to document the complete survey context and were outside the scope of the present analysis.*

1. Invitation letter

December 2025

Request for your cooperation with the “Questionnaire survey on the non-launch and development promotion of generic medicines”

We hope this message finds you well.

As part of the Health Labour Sciences Research Grant project funded by the Ministry of Health, Labour and Welfare (MHLW), “Research to inform the design of measures to promote development toward securing a stable supply and a sustainable industry structure for generic medicines” (Principal Investigator: Hiroaki Mamiya; Co-investigator: Ken-ichi Izutsu), we are conducting a fact-finding survey on cases in which generic medicines have not been brought to market. Although many generic medicines have been developed and supplied to date, a considerable number of products for which there is a certain level of demand are nevertheless not available on the market (non-launch).

The purpose of this research is to clarify the challenges in generic medicine development and to examine measures for addressing them, thereby supporting companies’ generic medicine development and ultimately contributing to the establishment of a stable supply system of generic medicines for the public.

We would therefore be grateful to hear about the actual circumstances and views of each generic medicine company, and we kindly ask for your cooperation with this survey. All responses will be processed statistically, and results will never be published in any form that identifies individual company names.

We appreciate that you are very busy, and we sincerely thank you for your cooperation.

How to respond

Web-based response: Please access the following site and enter the required information (Google Form). The original survey URL has been omitted because the survey is closed.

Response deadline: We would appreciate your response by Tuesday, 3 February 2026.

Contact: Hiroaki Mamiya, Laboratory of Pharmaceutical Policy and Evaluation, College of Pharmaceutical Sciences, Ritsumeikan University, 1-1-1 Noji-Higashi, Kusatsu, Shiga 525-8577, Japan; E-mail: h-mamiya@fc.ritsumei.ac.jp

2. Questionnaire

(Responses were collected via the web.)

Section 1: About your company

Q1. Please select the one option that best describes your company's principal business type.

- Generic (GE) manufacturing and sales-focused (domestic-capital company)
- Generic manufacturing and sales-focused (foreign-capital company)
- Originator-affiliated generic subsidiary
- Handles both new drugs (including long-listed products) and generics
- OTC-medicine-focused
- Mainly handles biosimilars (BS)
- CMO/CDMO
- Other (please specify: _____)

Q2. Please select the option closest to your company's annual sales of prescription pharmaceuticals in Japan (most recent fiscal year).

- Less than 1 billion JPY / 1 to <5 billion / 5 to <10 billion / 10 to <30 billion / 30 to <50 billion / 50 to <100 billion / ≥100 billion JPY

Q3. Please select the option closest to the number of generic medicines for which your company holds marketing approval in Japan (excluding different strengths of the same product).

- 0 / 1–10 / 11–20 / 21–50 / 51–100 / 101–200 / 201 or more

The following sections are to be answered by companies that hold approval for at least one generic medicine.

Section 2: Actual state of development discontinuation / non-launch

Q4. During the past five fiscal years (FY2020–2024), among products that were under development (including joint development) as generic medicines, have you had any case in which you ultimately discontinued development (including abandonment at the consideration stage) or, after obtaining approval, decided not to launch the product?

- Yes / No

Q5. (Only for companies answering “Yes” to Q4) Have you experienced development discontinuation or non-launch for products corresponding to so-called “generic drug loss” (e.g., a large originator market exists but no generic is developed; or generics are available overseas but not introduced in Japan)?

- Yes / No
- If “Yes,” specific details (optional): _____

Section 3: Reasons for discontinuation / non-launch (to be answered only by companies answering “Yes” to Q4)

Q6. To what extent do the following [broad factor domains] influence your company's decision to discontinue development or forgo launch? (For each item, select one: 5 = very strong influence, 4 = strong influence, 3 = some influence, 2 = little influence, 1 = no influence, 0 = unknown.)

- Q6-1. (1) Market viability and profitability problems
- Q6-2. (2) Formulation-technology and manufacturing difficulty (including patents)
- Q6-3. (3) Regulatory and clinical-study hurdles
- Q6-4. (4) Distribution and management-cost challenges
- Q6-5. (5) Competition (AG, etc.) and institutional uncertainty
- Comment (optional): _____

Q7. The following questions concern [specific factor items].

Column A: whether you have experienced the item as a reason for discontinuation or non-launch (1 = yes, 2 = no).

Column B: importance as a factor hindering generic medicine development (5 = very important, 4 = important, 3 = neutral, 2 = not very important, 1 = not important, 0 = unknown).

(1) Market viability and profitability

- Q7-1. Small originator market size (difficulty recovering development costs)
- Q7-2. Originator price (expected reimbursement listing price) is too low
- Q7-3. Rapid price erosion after launch
- Q7-4. Rapid market shifts, e.g., in oncology
- Q7-5. Obligation to supply low-demand strengths (e.g., pediatric strengths)
- Q7-6. Uncertainty over whether an authorized generic (AG) will be launched after approval
- Q7-7. Poor expected profitability due to AG market dominance
- Comment (optional): _____

(2) Formulation-technology and manufacturing difficulty

- Q7-8. Special formulation technology required
- Q7-9. High dedicated-equipment investment required
- Q7-10. Unclear equivalence-evaluation criteria for modified-release (DDS) and similar products
- Q7-11. Development/procurement cost of special devices (e.g., self-injection kits)
- Q7-12. Difficulty avoiding API patents (e.g., crystal-form patents)
- Q7-13. Difficult API procurement (price, quality, supply volume, etc.)
- Comment (optional): _____

(3) Regulatory and clinical-study hurdles

- Q7-14. Patient-based bioequivalence (BE) or clinical study (e.g., PD study) required
- Q7-15. Increasing number of cases requiring clinical studies
- Q7-16. Japan-specific additional studies (e.g., Japanese PK studies) required even when approved overseas
- Q7-17. Cost of meeting Japan-specific regulatory requirements (stability testing, API/excipient specifications, etc.)
- Q7-18. Differences in overseas handling, e.g., salt changes not being accepted
- Q7-19. Insufficient opportunity for dialogue with regulators, e.g., limits on the number of PMDA consultations
- Q7-20. Overseas BE/stability data not accepted as-is
- Q7-21. Lack of product-specific guidance such as the FDA PSG
- Comment (optional): _____

(4) Distribution and management-cost challenges

- Q7-22. Cost of building and maintaining proper-use and distribution-management systems (e.g., for narcotics)
- Q7-23. Special packaging/logistics costs (large boxes, aluminum single-dose blisters, etc.)
- Comment (optional): _____

(5) Competition and institutional uncertainty

- Q7-24. Reduced marketability due to concerns about AG launch
- Q7-25. Entry deterrence by an AG obtaining approval but not being launched
- Q7-26. Opacity of patent linkage (patent-judgment risk)
- Q7-27. Five-year stable-supply obligation after launch (including the risk associated with the written pledge) and difficulty of discontinuation

- Comment (optional): _____

Section 4: Views on market structure and entry

Q8. What number of entrants per generic active ingredient do you consider appropriate?

- Oral products: 3 companies / 5 / 7 / 8 or more / Other (please specify)
- Injectable products: 3 companies / 5 / 7 / 8 or more / Other (please specify)
- Topical products: 3 companies / 5 / 7 / 8 or more / Other (please specify)
- Comment (optional): _____

Section 5: Importance of measures for development promotion and industry-structure improvement (general measures)

Q9. Please rate the importance of each of the following measures from the perspective of promoting generic medicine development and improving industry structure. (For each item, select one: 5 = very important, 4 = important, 3 = neutral, 2 = not very important, 1 = not important, 0 = unknown.)

(1) Reform of the drug pricing system

- Q9-1. Abolition (or review) of off-year price revisions
- Q9-2. Reflecting inflation, labor costs, and material costs (including raising minimum prices)
- Q9-3. Abolition of the three-price-band system for generics (return to brand-by-brand listing)
- Q9-4. Improving the effectiveness of unprofitable-product repricing and adding flexibility to the withdrawal (price-deletion) process
- Q9-5. Preferential pricing for products requiring clinical studies and for complex generics
- Q9-6. Introducing minimum prices for dosage forms without them (e.g., ophthalmic and topical products)
- Q9-7. Pricing measures for low-volume strengths (e.g., pediatric low-dose strengths)
- Q9-8. Pricing measures for low-volume formulations (e.g., pediatric dry syrups)
- Q9-9. Pricing measures for device costs (e.g., self-injection kits)
- Comment (optional): _____

(2) International harmonization and deregulation

- Q9-10. International harmonization of BE guidelines
- Q9-11. Acceptance of all or part of the overseas BE / application package
- Q9-12. Ensuring consistency with overseas practice at the operational level in line with the ICH M13A guideline
- Q9-13. Mutual recognition of API/excipient standards (USP/EP, etc.)
- Q9-14. Review of Japan-local requirements such as stability testing
- Comment (optional): _____

(3) Support for specific products and technology areas

- Q9-15. Expansion of subsidies/funds for special manufacturing equipment (e.g., OROS)
- Q9-16. Provision of incentives for generic development of pediatric formulations
- Q9-17. Complex generics support (development of product-specific guidance [PSG]; pricing preference)
- Comment (optional): _____

(4) Improvement and transparency of regulatory and institutional operation

- Q9-18. Increasing transparency of patent linkage
- Q9-19. Expansion of the PMDA consultation system (more face-to-face advice slots; faster turnaround)

- Q9-20. Increasing transparency of the AG system (mandatory disclosure of intent to launch after approval; consideration of allowing application routes other than repackaging)
- Q9-21. Change in the insurance handling of AGs
- Q9-22. Simplification of discontinuation procedures for products of low medical necessity
- Q9-23. Clarification of approval requirements for salt-change development of active ingredients
- Comment (optional): _____

(5) Other items toward a sustainable industry structure

- Q9-24. Review of the all-strength supply obligation (all-strength requirement)
- Q9-25. Support for equipment-renewal costs (pricing measures or subsidies)
- Q9-26. Review of joint-development and repackaging rules to reduce low-volume, high-variety production
- Q9-27. Promoting appropriate product selection through formularies
- Q9-28. Human-resource development for manufacturing and quality control
- Comment (optional): _____

Section 6: Specific scenarios for particular measures

Q10. For complex generics and generics requiring clinical studies (patient studies, PD studies, long-term clinical studies, etc.), are there products that your company would be able to develop if the drug price were simply “increased by 10%”?

- Yes / Limited yes / No / Don’t know
- Comment (optional): _____

Q11. If a hybrid approval scheme similar to the US 505(b)(2) pathway were introduced, would there be room to develop products currently subject to “generic loss”?

- Room exists / Limited room / No room
- If “Room exists,” please describe the relevant therapeutic areas or products (free text).

Section 7: Free description

Q12. Please list specific regulations or systems that you consider to be Japanese “local rules.”

Applicable document no.	Document name	Applicable section	Situation in other countries	Improvement proposal and rationale

Q13. Please describe the initiatives that you consider necessary to address non-launch and to promote the development of generic medicines (free text).

Q14. Please describe any overall opinions or comments (free text).