

Mapping Quality-of-Life Instruments in Japanese HTA Submissions: Current Practices and Future Directions

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INTRODUCTION

- Japan's health technology assessment (HTA) framework, overseen by the Center for Outcomes Research and Economic Evaluation for Health (C2H), places strong emphasis on the use of EQ-5D-based utility values for cost-effectiveness evaluation.
- In principle, EQ-5D-5L utilities derived using Japan-specific tariffs are preferred, reflecting methodological guidance and known cross-country differences in health state preferences.
- However, in many clinical development programs, EQ-5D data are not collected. In such cases, mapping from alternative quality-of-life (QoL) instruments is permitted within Japanese HTA submissions.
- Despite the practical importance of mapping in Japan, empirical evidence describing how mapping has been applied in completed C2H submissions, and how these approaches have been received by reviewers, remains limited.
- A clearer understanding of real-world mapping practices and recurring methodological concerns may help inform future study design, analysis planning, and HTA submissions.

OBJECTIVES

To systematically review published C2H summary reports and characterize the use of mapped utilities, including source instruments, target EQ-5D measures, tariff selection, and associated C2H feedback.

METHODS

Study Design and Data Sources

A structured review was conducted of completed HTA submissions published by C2H between April 2019 and September 2025, based on publicly available HTA summary reports.

Screening

Submissions were screened to identify cases in which health state utilities were derived using mapping techniques. Mapping use was identified through descriptions of utility derivation methods within the HTA documentation.

Data Extraction

For each submission employing mapped utilities, the following was extracted:

- Source instrument, categorized as generic or disease-specific
- Target utility measure
- Tariff selection, including whether Japan-specific value sets were used
- Complexity of mapping strategy
- C2H feedback, specifically:
 - Methodological concerns related to mapping
 - Requests for additional analyses or re-analyses

Analysis

Extracted data were summarized descriptively to identify patterns in mapping practices and recurring themes in C2H reviewer concerns.

RESULTS

40 HTA submissions were identified, of which 10 submissions (25%) used mapping to derive utility values

- 4 mapped from generic instruments
- 6 mapped from disease-specific instruments

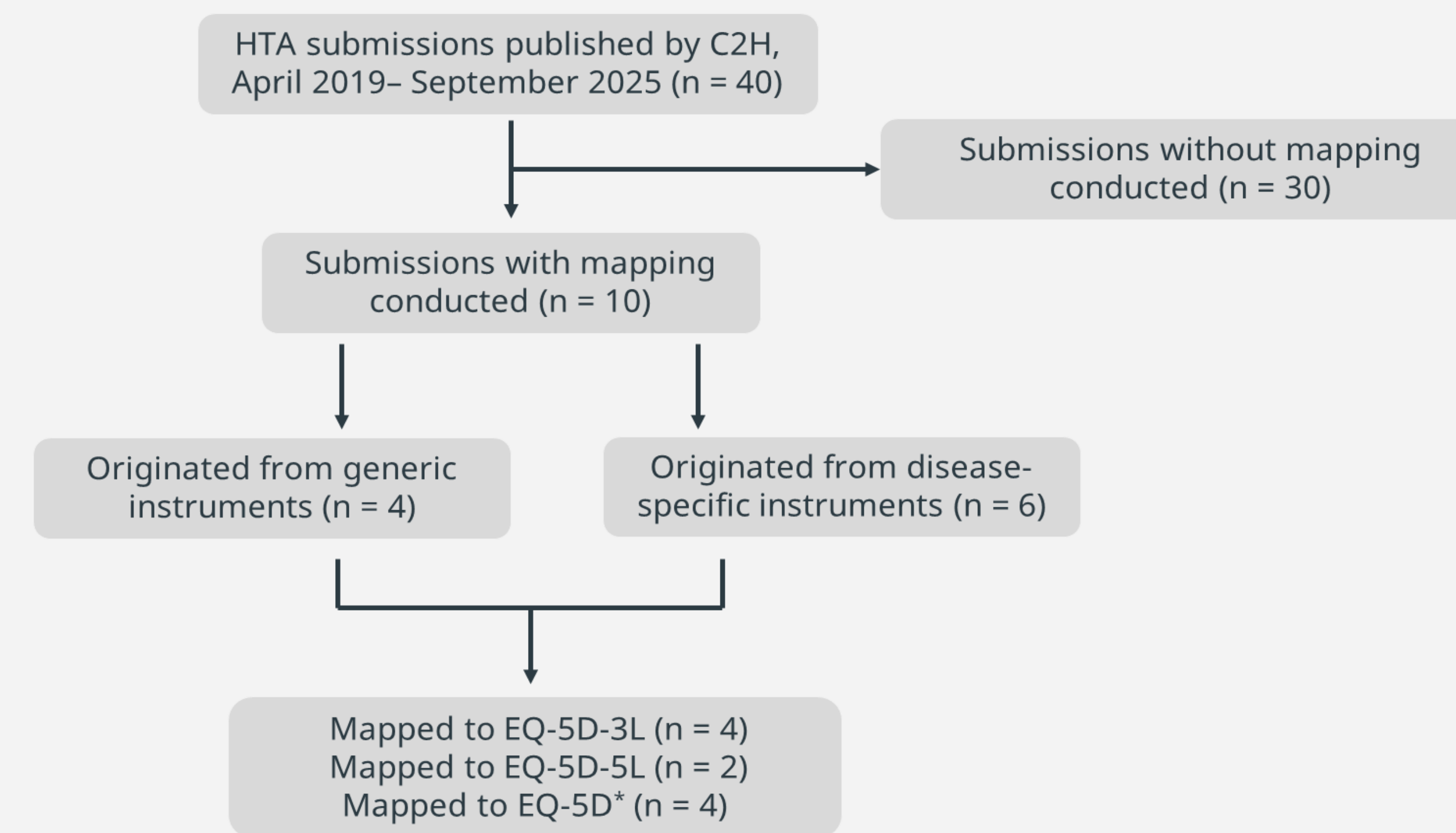


Figure 1. PRISMA Diagram

- EQ-5D version unspecified (EQ-5D*) was the most common mapping target, used in 4 of 10 submissions (40%)
- SF-36 was the most common source instrument, used in 4 of 10 submissions (40%), followed by EORTC QLQ-C30 in 3 of 10 submissions (30%)

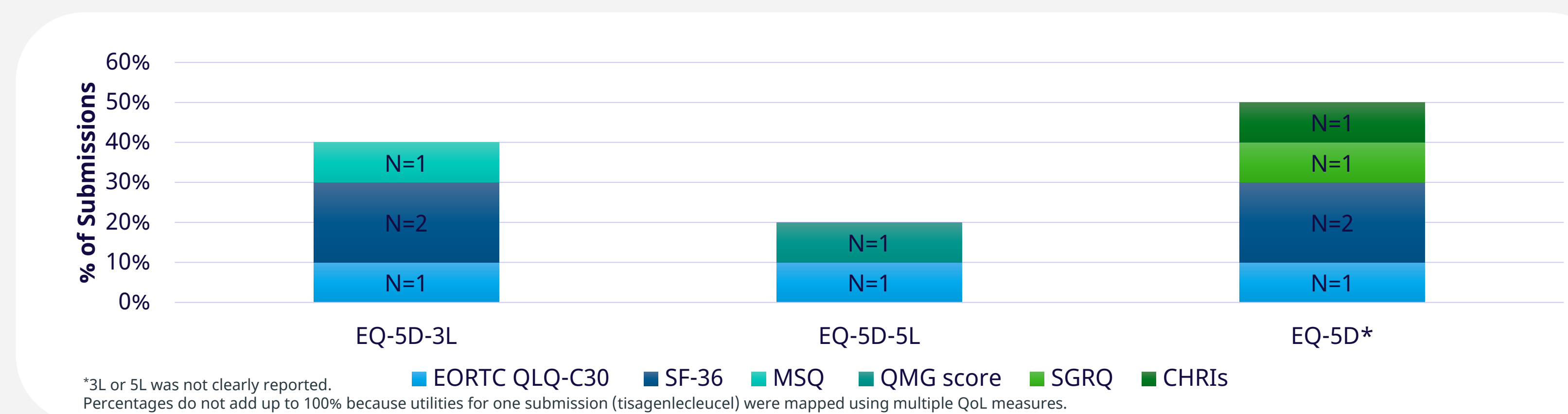


Figure 2. Distribution of QoL measures mapped to EQ-5D-3L, EQ-5D-5L and EQ-5D* among total mapping submissions

- 9 of 10 submissions (90%) using mapped utilities raised explicit C2H concerns, but only 5 of 9 led to a QoL-related public re-analysis.
- Re-analysis occurred selectively, most often when observed EQ-5D data or clear alternative approaches were available, or when mapping showed clear conceptual issues (e.g., mixed instruments, recall misalignment).
- 4 cases raised concerns without re-analysis, typically when no directly measured EQ-5D data existed, limitations were considered unavoidable, and mapped utilities were viewed as sufficient for qualitative interpretation.
- Japan-specific mapping approaches were rare but consistently accepted, either without re-analysis (e.g., luspatercept) or after re-analysis when newly developed (e.g., selpercatinib).
- In contrast, non-Japanese algorithms or tariffs were a common source of concern and more likely to prompt re-analysis when feasible alternatives existed.

Table 1. Overview of Utility Mapping Approaches and C2H Concerns

Drug	Company Mapping Method	Tariff Used	Concerns Identified	QoL-Related Public Re-Analysis	Accepted Instrument
Luspatercept	EORTC QLQ-C30 → EQ-5D-5L [1]	Japan	Mapping was based on a Japan-specific algorithm and considered acceptable. However, concerns remained regarding representativeness of Japanese patients at life-expectancy extremes in the trial population.	None	EQ-5D-5L
Semaglutide	SF-36 → EQ-5D-3L (source not reported)	UK	Mapped SF-36-based QOL values using non-Japanese tariffs raised applicability concerns, but were accepted due to the absence of alternative evidence in Japanese patients.	None	EQ-5D-3L
Efgartigimod alfa	QMG score → EQ-5D-5L [2]	Foreign unspecified	Mapping relied on an overseas QMG-to-EQ-5D algorithm, raising concerns about applicability and alignment with EQ-5D-5L values observed in the ADAPT trial.	None	EQ-5D-5L
Galcanezumab	MSQ → EQ-5D-3L [3]	UK	MSQ-to-EQ-5D mapping relied on an overseas algorithm and point-in-time health status, raising concerns regarding population applicability and conceptual validity.	EQ-5D-5L scores from the CGAW trial were regressed on MHD to derive MHD-specific utilities, which were used in the base-case analysis.	EQ-5D-5L
Polatuzumab vedotin	SF-36 → EQ-5D (source not reported)	UK	Mapped QOL values were seen as less appropriate than directly measured, preference-based QOL data available from the ZUMA-1 trial, despite limitations in sample size and population composition.	EQ-5D scores from the ZUMA-1 trial were used, with age-related QOL decrements applied to health states.	EQ-5D-5L
Micra AV	SF-36 → EQ-5D-3L [4]	UK	QOL estimates were subject to uncertainty because the mapping algorithm was derived from a population different from the target cohort, and one key SF-36 data source lacked covariate adjustment, raising concerns about the validity of the utility inputs.	QOL values were recalculated using SF-36 summary scores from the Palmisano study and converted to EQ-5D using the same mapping algorithm as the sponsor.	EQ-5D-3L
Selpercatinib	EORTC QLQ-C30 → EORTC-8D → EQ-5D-3L [5-8]	UK [6,8] Greek [7]	Mapped utilities depended on non-Japanese reference data and algorithm choice, raising concerns regarding applicability to the Japanese population.	A Japan-specific mapping algorithm was used to convert QLQ-C30 to QLQ-LC100, and recalculated utilities were adopted in the reanalysis despite variability in PD-specific QOL data.	EORTC QLQ-LC100
Fluticasone furoate, umecclidinium, and vilanterol	SGRQ-C → SGRQ → EQ-5D [9-10]	UK	Treatment-specific QOL differences were derived through multi-step modeling and mapping, despite the absence of demonstrated EQ-5D differences between treatments, raising concerns about the validity and magnitude of the assumed utility differences.	None	EQ-5D
Tisagenlecleucel	SF-36 → HUI2; CHRIS → EQ-5D, HUI2 [11-12]	CA [11] US [12]	Generic QOL measures (SF-36, CHRIS) were mapped to preference-based utilities (HUI2, EQ-5D), resulting in mixed instruments and raising concerns regarding conceptual consistency and validity.	EQ-5D-3L utilities reported by Laetsch et al. from the ELIANA trial were used as QOL inputs for the base-case reanalysis.	EQ-5D-3L
Ravulizumab	QLQ-C30 → EQ-5D (source not reported)	Not reported	None	CMA conducted due to no benefit	None

CONCLUSIONS

- Mapping remains a commonly used and often necessary approach for deriving health state utilities in Japanese HTA submissions when EQ-5D data are unavailable or deemed inappropriate for the disease state.
- However, this review highlights persistent methodological challenges, including limited transparency of mapping methods, frequent reliance on non-Japanese tariffs, and the use of multi-step conversion pathways from disease-specific instruments to EQ-5D utilities.
- These issues complicate interpretation of cost-effectiveness results and have prompted concerns and requests for re-analysis by C2H during appraisal.
- Despite recognition of these limitations, practical alternatives remain constrained by data availability and the lack of validated Japan-specific mapping algorithms.
- Greater clarity in the reporting of mapping pathways, explicit justification of tariff choices, and development of Japan-specific mapping approaches may help reduce uncertainty and improve alignment with C2H expectations in future HTA submissions.

Conflicts of Interest

All authors are employees of IQVIA Solutions Japan G.K. and have no conflicts of interest to disclose.

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