March 16, 2023

Cabinet Secretariat
Office for COVID-19 and Other Emerging Infectious Disease Control

Health and Global Policy Institute (HGPI)

Opinions Regarding the Proposed
"National Action Plan on Antimicrobial Resistance 2023-2027 (Draft)"

Since Japan's National Action Plan on Antimicrobial Resistance (AMR) came into effect in 2016, efforts to combat AMR have been made by the Government of Japan as well as through joint action from industry, government academia, and civil society. In addition to measures taken within its borders, Japan must continue leading global efforts against AMR in its capacity as a G7 member. Looking ahead to the 2024 UNGA High-level Meeting on AMR, we offer the following four recommendations for consideration during the formulation of the National Action Plan on AMR (2023-2027) ("the next NAP").

Recommendation 1: Revision of package inserts should be proactively considered taking into account the actual situation at health care facilities (Related to Goal 2)

Recommended dosing for antimicrobials, etc. is specified in the package inserts prepared by pharmaceutical companies, but this information sometimes differs from the information in guideline. For example, for treatment of pneumonia, guidelines recommend prescribing Amoxicillin at 1500 milligrams to 2000 milligrams per day (500 milligrams per dose, 3-4 times daily), but the package insert for the drug specifies 1000 milligrams per day as the maximum dose. Among certain broad-spectrum antimicrobials, relatively new agents have lower bioavailability, which also calls into question the appropriateness of package insert information. A revision of package inserts that takes into account the actual situation at healthcare facilities should be undertaken by MHLW as a regulatory authority and by pharmaceutical companies. Antimicrobial stewardship at medical institutions should be supported by correct information.

Recommendation 2: The Government should take the lead in creating and standardizing English names used within the medical service fee system and for related items and by establishing master databases for data related to healthcare and pharmaceuticals (Related to Goals 2, 3, and 6)

Providing the world with standardized information in English and Japanese will be essential when working to verify the effectiveness of policies and to successfully establish new evidence through research. For example, official English names should be assigned to recently-established premiums such as the "Premium for enhanced outpatient infection control measures," "Premium for enhanced cooperation," and "Premium for enhanced surveillance" to reflect the purposes of these systems as well as their actual mechanisms. An overview of the medical service fee system should also be provided in English. Such actions are likely to contribute to the global dissemination of good examples of AMR control measures originating from Japan. These examples include guidelines like the *Manual of Antimicrobial Stewardship* as well as parts of the medical service fee system, where premiums like the "Premium for supporting pediatric antimicrobial stewardship" have already demonstrated a certain degree of effectiveness. While keeping pace with efforts to standardize data held in electronic medical records and other ongoing reforms for digital transformation (DX) in healthcare, steps must be taken to establish master databases for healthcare and pharmaceutical-related data as well as to ensure databases are versatile. Plans for linking each database starting with the National Database of Health Insurance Claims and Specific Health Checkups of Japan (NDB) with surveillance data should be in place from the time those databases are first established. In addition to advancing domestic AMR control, proactive efforts in this area from the Government of

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Japan will also provide leadership in AMR countermeasures at the global level, particularly in the Asian region.

Recommendation 3: Steps should be taken to develop human resources and establish an environment to facilitate proactive AMR screening, microorganism identification, and drug susceptibility testing (including genetic testing through nucleic acid amplification tests) (Related to Goals 1, 2, and 5)

Operating and managing equipment for and interpreting the results of AMR screenings and rapid diagnostic testing require high levels of technical skill. However, increased healthcare demand and personnel shortages have resulted in cases where tests must be conducted by health professionals other than clinical technologists. Items that should be considered in light of these circumstances include introducing simplified, automated testing devices that do not require technical expertise to operate and creating easy-to-understand guidelines for operating and managing testing equipment and interpreting results. The *Manual of Antimicrobial Stewardship* compiled by the Ministry of Health, Labour and Welfare (MHLW) and other organizations provides one good example of this. It has been used by many health professionals to a certain degree of effectiveness, and could be introduced in low- and middle-income countries where health resources are limited.

Testing requires a comprehensive package of resources including testing equipment, reagents, materials, Personal Protective Equipment (PPE), facility equipment like safety cabinets and ventilation, and human resources. While some of these are disposable, such as PPE or the materials required for testing, the information obtained from those tests can be stored in a semi-permanent manner in surveillance systems at the national, regional, or local levels, or at healthcare institutions. As such, an environment that provides a constant, stable supply of products that are superior in all aspects including quality, quantity, price, and specifications must be established to facilitate testing. Currently, there are times when test specimen selection is influenced by the country conducting development, or cases in which diagnostic reagents that are not approved as in vitro diagnostics are being used to conduct testing. While taking steps to ensure compliance with conditions for use, criteria must be updated and examined to determine if they are in line with Clinical and Laboratory Standards Institute (CLSI) guidelines and with current circumstances in Japan.

Diagnostic stewardship makes AMR countermeasures and antimicrobial stewardship possible through the effective use of new items in the medical service fee schedule like the “Premium for enhanced outpatient AMR countermeasures and coordination.” From the perspective of diagnostic stewardship, it will be essential to establish an environment for fostering and developing human resources like clinical microbiologists and other specialists in infectious disease control. We hope to see intensified efforts in this area moving forward.

Recommendation 4: When providing final evaluations, the National Action Plan should include both outcome and process indicators that can used in a manner that allows for comparisons by regional characteristics (Related to National Action Plan performance indicators)

The next NAP should include indicators that assess behaviors at each stage of AMR control measures (“process indicators”) and indicators that assess the final results of AMR control measures (“outcome indicators”) in line with each long- and short-term target. For example, two outcome measures could be considered; the lower number of patients infected with antimicrobial resistant organisms (based on NESID) and the lower number of deaths from antimicrobial resistant infections (based on vital statistics). At the same time, it will also be necessary to establish indicators and initiatives that take the latest findings from research and other sources into account for urinary tract infections and other diseases that are difficult to link to the number of deaths but

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do pose medical and disease burdens. (An example of one such study can be found at https://www.bmj.com/content/380/bmj-2022-072319.long.)

An analysis should be carried out on trends in antimicrobial resistance rates and antimicrobial use for each bacterial species throughout the NAP 2016-2020 timeframe. This should include analysis of the relationship between antimicrobial use and resistance rates, and the relationship between oral antimicrobial and intravenous antimicrobial use in the human sector. This analysis should take place on a rolling basis, and outcome indices in the next NAP should be set and revised in accordance with analysis results.

In particular, numeric targets need to be set based on evidence. Diagnostic tests are indispensable for distinguishing between the proper and improper use of antimicrobials. Point-of-care testing (POCT) should be promoted concurrently with numerical targets in order to evaluate the appropriate use of antimicrobials and to encourage antimicrobial stewardship. When setting each indicator and target, it is important to recognize that there are regional variations in antimicrobial use and the distribution of antimicrobial resistant bacteria. Consideration should be given to frameworks for information collection, evaluation, and assessment on a prefecture, primary or secondary care area, healthcare institution, or prescriber basis.

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