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Re: Public Comment on the Progress Report: Implementation of a Public Health Action Plan to Combat Antimicrobial Resistance: Progress through 2008
FR Doc.2010-1570

The Alliance for the Prudent Use of Antibiotics (APUA) would like to recognize the CDC, the FDA, the NIH, the Interagency Task Force on Antimicrobial Resistance, and the authors of the *Public Health Action Plan to Combat Antimicrobial Resistance* for their substantial progress in addressing U.S. domestic antibiotic resistance (ABR) issues.

Founded in 1981 as a global non-profit organization, APUA's mission is to promote appropriate antimicrobial access and use. Based on our network of experts in the private sector, APUA works closely with government agencies to provide objective information to guide antimicrobial supply, treatment, and policy decisions. APUA programs are designed to maximize treatment effectiveness for patients by: (1) increasing public awareness and knowledge about ABR; (2) improving institutional and governmental antimicrobial policies; and (3) promoting microbiology, surveillance and diagnostics capacity (See www.apua.org).

APUA offers the following comments on the Action Plan and the Progress through 2008 Report. We look forward to lending our support and expertise to assist the agencies in implementing action plan projects, and we are pleased to discuss any comments further with the reviewing committee and the Task Force.

General Comments:

Need for More Program Synergy and Coordination: The breadth of activity is very impressive. The agencies are to be congratulated for the increased attention to the problem of resistance and many powerful programs listed. Having one list of the progress summaries for each of the many federal venues that relate to antimicrobial resistance coordination is very helpful. However, when the Interagency Task Force was established, the hope was that it could actively coordinate all of those programs to develop synergies, reduce duplication and integrate their findings. This expectation was a basis for the Task Force receiving the APUA Leadership Award in 2002. This progress report does not present much evidence for such coordination beyond what had been built into the programs themselves (e.g. NARMS). Dedicating a small percentage of the total effort of all the programs towards active collaboration would still seem cost-effective and, potentially, enhancing.

Towards this end, the agencies could meet on an annual or biannual basis to establish priorities and analyze policy implications resulting from their research findings. The findings and recommendations could then be conveyed to relevant federal authorities. To increase the relevance and impact of the plan, any research project undertaken should be chosen based on priority policy questions to be addressed, and then linked back to policy implications. Studies should be published soon after completion and a list of publications from each would be helpful.

The fact that there are multiple agencies responsible for taking an item forward may lead to stagnation, where none of the listed organizations advance the action. One agency should be designated as the 'lead' for each item listed in the plan and in the progress report.

Need to Prioritize Action Items: No budgetary estimate is provided for the top priority action items listed. Identifying 2-3 action items from within the 13 priorities may be more helpful. Furthermore, without some estimate of what the cost of implementation would be for these action items, prioritizing among the 13 will be difficult. Some of the proposed actions are much more costly than others, e.g. to develop new antibiotics is much more costly than to conduct a public health campaign to promote appropriate antimicrobial use. Page 11 (paragraph 4) states, "The plan will be implemented incrementally as resources become available." With incremental resources, the danger is that the easier and cheaper - but not necessarily the most important – initiatives will be pursued first. Consequently, valuable time might be lost in this way. The Progress Report does not provide any budgetary estimates or costs of implementation for the projects listed under each action item.

Comments on Specific Issues and Items:

ABR Cost: On page 10 (paragraph 1), the plan states that "it has been estimated that the in-hospital cost of hospital-acquired infections caused by just six common kinds of resistant

bacteria are at least $1.3 billion, in 1992 dollars." This figure is a woeful underestimate. Providing an up-to-date cost (in 2010 dollars) would be more helpful; using a conversion factor of 1.57 for 2010, the cost listed in the plan would be approximately $2 billion. However, based on a recent APUA-initiated study with Cook Country Hospital*, we believe the amount to be closer to $25-30 billion - a tenfold difference. More efforts to address this important issue and establish the true cost of antibiotic resistance to the U.S. would help in generating the required financial resources to truly tackle these priorities as outlined. Action item no.16 (p. 18) addresses this issue, but the difficulties of obtaining reliable data linking costs to specific ABR organisms other than MRSA are under-appreciated. An updated overall cost estimate of resistance in the U.S. (perhaps in an introductory section of the Progress Report) would be helpful, alongside the budgets for the implementation of individual projects.

*Study Citation: Roberts RR, Hota B, Ahmad I, et al. Hospital and societal costs of antimicrobial resistant infections in a Chicago teaching hospital: implications for antibiotic stewardship. Clin Infect Dis 2009;49:1175–84
(Available at: http://www.journals.uchicago.edu/doi/pdf/10.1086/605630)

Prevention and Control: In the section on Prevention and Control (p.20, 24) in the action plan, one set of drivers of physician behavior is the reimbursement patterns for physician visits and lab tests, particularly in the outpatient setting. Anecdotal information suggests that some insurers encourage the presumptive prescription of antibiotics, both to reduce lab test costs and reduce the need for a second visit. This matter needs to be investigated and quantified, and, if true, appropriate measures need to be taken to inform and educate the insurance industry, as well as health administrators and government payers of the costs and effects of these practices. Action item no. 34 (p. 24) refers to the barriers to testing, but the other potential barrier is the pressure on clinician time and the potential 'savings' by both presumptive prescribing and reduction of second visits. The progress report does not yet include any projects under action item no. 34. This issue would also impact the implementation of projects under priority action item no. 26 (p. 22), education for clinicians, and under action item no. 32 (p.23), appropriate use in managed care organizations.

Priority action item no. 58 (p.29-30) specifies that the requirements for the industry's submission of drug use data will be revised. The current requirements and the expected new requirements should be indicated in both the action plan and in the projects under priority action item no. 58 in the progress report. Even though the projects are listed as 'initiated' in the action plan, the progress report does not show evidence that work is being conducted in this area. The question remains of what the differences will be between the present and future industry requirements for drug-use data submission. Since antibiotic use is considered a major selective pressure driving resistance, collection of data on antibiotic use in both human medicine and agriculture needs to be a top priority.

Use of these data combined with longitudinal data on resistance trends and patterns are needed to provide baseline measurements of the problem, as well as input of interventions. Use of antibiotics in food animal production and residues in the environment are priority areas that are understudied and unregulated. The EPA, FDA, and CDC should be funded to establish more aggressive surveillance and regulatory programs to address the broad public health impact of the

high selective pressures from antibiotic use in agriculture. The EU has invested more funding and coordinated scientific resources to address increasing antibiotic resistance. As a result they have working systems and models to collect and analyze ABR data and apply them to public health policy. This larger scale focus on ABR provides many lessons and models that could be emulated. U.S. citizens are entitled to the same protections from excess antibiotic selective pressure as are EU citizens.

In regards to action item no. 35: "In collaboration with professional societies, industry, health departments, and other stakeholders and partners, develop guidelines for clinicians and clinical microbiology laboratories" (p.24). This action item is a priority need to establish guidelines and materials from CDC and their professional associations. APUA focus groups of physicians have identified a need for government and associations to provide support for appropriate "non prescription" of antibiotics to help them "do the right thing." More agency publications, guidelines and constant communication are needed to support US physicians in improving prescribing patterns. The successful US pediatric campaign to raise awareness and improve pediatric prescribing should be studied as a model and replicated in other specialties, such as surgery and adult medicine. As a top priority item, CDC should work with IDSA and other groups to accelerate release of updated guidelines; otherwise, unnecessary selective pressure from inappropriate use will render ineffective both existing and new agents.

Since patient pressure is a key reason cited for over-prescription, patient education needs to be supported. In regards to patient education, an APUA survey of over 2,000 primary care doctors found that patient pressure is a primary factor in their prescriptions for antibiotics. Of these physicians, 93% admitted that physicians overprescribe antibiotics; this problem presents an intervention opportunity.

Access to New Antibiotics: The evidence of the effectiveness of many existing interventions in slowing antibiotic resistance is limited, and, simultaneously, the pipeline of antibiotics is diminishing. As a result, the need to develop new antibiotics eclipses other priorities. Nevertheless, developing novel antibiotics is probably the most costly intervention and takes the most time to implement. In the same vein, action item no. 81 (p. 39) - considering "whether government has a constructive role to play in discovery of drugs" – is, in our view, an urgent priority. Based on the progress report, the current projects under action item no. 81 focus primarily on vaccine development; no projects are centered on novel antibiotic development. Also, financial incentives to the private sector should be instituted to promote development of priority drugs, such as those for targeting ESBLs, as well as new classes of drugs that can circumvent existing resistance mechanisms or have new targets. More is not better. Prioritizing needs would send a message to the private sector as to which agents to pursue.

Surveillance: Surveillance of ABR and antibiotic use in both humans and animals should be an ongoing top priority. Considering the progress report of the projects being conducted for priority action item no. 5 and the activities outlined in the action plan (page 16), we suggest: (1) that the efforts to "link human drug-use data to clinical information" be extended to companion animals, live stock, and the environment; (2) that resistance patterns in animals, humans, and the environment be added to the plans to "link agricultural drug-use data to species and usage

patterns;" and (3) that ongoing longitudinal surveillance of resistance be instituted for priority pathogens.

With respect to action item no. 17 (p.19), the progress report does not indicate that surveillance is being conducted for organisms not usually transferred via the food chain, for example, MRSA. Even though MRSA is being examined through projects in healthcare facilities, enhancing food chain surveillance and environmental surveillance to include MRSA and other organisms not generally transferred via food is important.

Additionally, pilot studies to assess the environmental contamination of air from agricultural areas– not simply water and soil, as noted in action item no. 19 (p.19) – should be added to the surveillance initiative. People living near industrial farm animal production (IFAP) sites suffer adverse effects due to poor air quality from the oversaturation of local fields with deposited manure.

Thank you.

APUA