CONSULTATIONS AND WORKSHOPS

Critically Important Antimicrobials for Human Medicine:

Categorization for the Development of Risk Management Strategies to contain Antimicrobial Resistance due to Non-Human Antimicrobial Use

Report of the Second WHO Expert Meeting
Copenhagen, 29–31 May 2007

DEPARTMENT OF FOOD SAFETY, ZOONOSES AND FOODBORNE DISEASES

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CONTENTS

Preamble

Executive Summary **1**

1. BACKGROUND **3**

1.1 WHO in the wider global context of containing antimicrobial resistance (AMR) 3

1.2 Containing antimicrobial resistance owing to human use of antimicrobials 3

1.3 Containing antimicrobial resistance owing to non-human use of antimicrobials 4

2. OVERALL OBJECTIVES AND OUTCOME OF THE MEETING **6**

3. INTRODUCTION **6**

3.1 What should the list be used for? 7

3.2 What should the list not be used for? 7

3.3 Important considerations 7

3.4 Geographical considerations 7

3.5 WHO Model List of Essential Medicines 8

4. UPDATING THE CANBERRA LIST **8**

4.1 Elements for consideration to update the Canberra list 8

4.1.1 Recent developments in antimicrobial resistance 9

4.1.2 WHO Expert Committee for the Selection and Use of Essential Medicines 10

4.2 Changes in this document compared to the Canberra document 11

4.2.1 Change in title 11

4.2.2 Re-examination of the list of all antimicrobial classes used in human medicine and categorization of antimicrobials 11

5. PRIORITIZATION WITHIN THE *CRITICALLY IMPORTANT* CATEGORY **21**

6. CONCLUSIONS **27**

7. RECOMMENDATIONS **27**

Annex 1: List of participants **31**

Annex 2: Agenda **33**

Preamble

The World Health Organization convened an Expert Meeting on Critically Important Antimicrobials for Human Medicine, in Copenhagen, Denmark, from 29 to 31 May 2007.

The meeting was organized to follow up a consultative process on critically important antibacterial agents for human health risk management strategies of non-human use (First WHO Expert Meeting on Critically Important Antibacterial Agents for Human Medicine, Canberra, February 2005), and a FAO/OIE/WHO consultative process on non-human antimicrobial usage and antimicrobial resistance (1st Workshop on Scientific Assessment, Geneva, December 2003, and 2nd Workshop on Management Options, Oslo, March 2004).

Following opening remarks delivered by Dr Jørgen Schlundt and Dr Awa Aidara Kane, of the World Health Organization, Dr Henrik Wegener welcomed participants on behalf of the National Food Institute, Technical University of Denmark. Professor Peter Collignon, of the Canberra Hospital, Australia, and Dr Ezra Barzilay, of the Centers for Disease Control and Prevention (CDC), Atlanta, USA, were elected as Chairperson and Rapporteur respectively.

Executive Summary

Antimicrobial resistance is a global public health concern that is impacted by both human and non-human antimicrobial use. The consequences of antimicrobial resistance are particularly important when pathogens are resistant to antimicrobials that are *critically important* in the treatment of human disease. WHO therefore convened a meeting of experts in Canberra, Australia, on 15 and 16 February 2005, to develop a list and categorization of drugs according to their importance in human medicine. Participants in that meeting categorized antimicrobial drugs as *critically important*, *highly important*, and *important* based on two criteria. When using these two criteria, participants categorized antimicrobials as critically important if they were: (i) sole therapies or one of few alternatives to treat serious human disease, and (ii) used to treat diseases caused by organisms that may be transmitted via non-human sources or diseases causes by organisms that may acquire resistance genes from non-human sources.

WHO convened the second WHO Expert Meeting on Critically Important Antimicrobials for Human Medicine in Copenhagen, Denmark, from 29 to 31 May 2007. Participants reviewed comments on the Canberra document that had been received from various parties including the WHO Expert Committee the Selection and Use of Essential Medicines. Comments indicated that the title of the document should include an explanation regarding the purpose of this list, so participants modified the title accordingly to indicate that the purpose of this list is for consideration as part of developing risk management strategies for antimicrobial resistance due to non-human antimicrobial use. The wording in the title was also modified from "antibacterials" to "antimicrobials" in order to be consistent with OIE listings and the concept that this list at present includes antibacterials but in the future may expand to include other agents.

The purpose of both the Canberra report and this report is to provide information on the human health consequences of antimicrobial resistance for use in the management of risk due to non-human use of antimicrobials. In addition, this information should be used to support more comprehensive assessments of risk. Such comprehensive assessments should include information on the potential development of resistance in pathogens in animals (release assessment) and the potential spread of resistant organisms or their genes from animals to humans (exposure assessment), and integrating these data into a comprehensive assessment of risk and strategies to manage that risk.

Participants reviewed the two criteria used to classify human antimicrobials at the first meeting held in Canberra and decided that these criteria remained appropriate. Participants then used those criteria to re-examine the categorization of all human antibacterial classes in light of new drug development and scientific information since 2005. On the basis of this re-examination, relatively few changes were needed to update the categorization of antimicrobials.

Participants were requested to prioritize agents within the *critically important* category in order to allow allocation of resources on the agents for which management of the risks from antimicrobial resistance are needed most urgently. For this, a more detailed application of the two original criteria was used than that employed to develop the Canberra list. Participants considered drugs of greatest priority when (i) there are relatively large absolute numbers of people affected with diseases for which the drug is the sole or one of few alternative therapies, (ii)) the overall frequency of use of the drugs in

human medicine for any use (whether appropriate or inappropriate) is relatively large, and (iii) the drug is used to treat disease due to pathogens for which there is a greater degree of confidence in transmission of bacteria or their genes from non-human sources to humans (*E. coli*, *Campylobacter* spp. and *Salmonella* spp.)

This prioritization resulted in the designation of the classes for which comprehensive risk management strategies are needed most urgently: quinolones, 3rd/4th generation cephalosporins and macrolides. Participants also emphasized that the prioritization of these three classes of drugs should not minimize the importance of other drugs categorized as *critically important* on the list.

Recommendations were provided to WHO on various aspects related to antimicrobial resistance in order to protect human health. It was pointed out that there are important gaps in our knowledge and that there is a need for better data on various factors that impact the assessment of risks from antimicrobial resistance due to non-human use as well as human use. There is a need for more and better information on burden of illness in relation to antimicrobial resistance attributable to non-human use of antimicrobials. There is also a need for data on antimicrobial utilization in both humans and animals, data on factors that lead to development and spread of antimicrobial resistance in various pathogens in animals and humans, and better data on the benefits of antimicrobials in both animals and humans in order to balance the benefits as well as the risks of antimicrobial use.

Participants also pointed out that the development of this list is part of a more comprehensive approach to the public health issue of antimicrobial resistance in both animals and humans. It was emphasized that there should be a sense of urgency to the development of such risk management strategies, particularly for quinolones, 3rd/4th generation cephalosporins and macrolides.