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REPORT OF THE WHO WORKING GROUP ON ANTIMICROBIAL RESISTANCE

Weybridge, United Kingdom, 4 December 1991

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INTRODUCTION

The meeting was held at the Central Veterinary Laboratory (CVL), Weybridge, UK and the WHO working group members as well as representatives of the European Animal Health Federation (FEDESA) were welcomed by Dr T.W.A. Little, Director of the CVL. The meeting was opened by Dr T. Fujikura, Veterinary Public Health, Communicable Diseases Division of WHO, on behalf of Dr Hiroshi Nakajima, Director General of the Organization. The list of participants is in Annex I.

Dr Fujikura explained the purpose and scope of the meeting:

- discussion of the steps to be taken by the working group in line with the contents of the WHO Guidelines (WHO/Zoonoses/90.167) elaborated by the group;

- discussion of work plans for 1992-1993 and identification of collaborative study areas for further international cooperation.

Dr Brinley Morgan was elected Chairman and Dr Wray served as Rapporteur.

1. MAJOR POINTS OF DISCUSSION

1.1 The Guidelines for surveillance and control of antimicrobial resistance (WHO/Zoonoses/90.167) had been distributed worldwide and many requests for additional copies had been and were still being received.

The group briefly reviewed the objectives of the Guidelines, listed below:

- selection of species of bacteria to be examined as indicators of antimicrobial resistance;

- selection of antimicrobial substances to be used for susceptibility testing;

- standardization of methods of testing for antimicrobial resistance and reporting systems; and

- an attempt to evaluate the factors influencing the increase in antimicrobial-resistant bacteria.

Whilst recording and reporting on antimicrobial resistance was important, it was stressed that this was only one ingredient by which the problem could be contained epidemiologically and at an early stage.

1.2 The need to provide simple techniques for resistance monitoring was stressed in order to facilitate the gathering of information, analyzing and summarizing the results. In this way, national authorities could be provided with summary information on the existing position and to predict potential problems. It is important, therefore, to cover human and animal health as well as the environment.

1.3 The possibility was stressed of selectively broadening membership of the group so as to take into account and reflect the intersectoral nature of the surveillance programme. The group would give consideration to other known laboratories as well as appropriate experts suggested by the current members. In the meantime the group would identify other possible laboratories for further cooperation. There is also a need to identify groups/laboratories able to assist in the development of enzyme assays and molecular markers of antimicrobial resistant strains. In this connection collaboration with FEDESA should also be maintained.

1.4 There was much discussion on the need for recommendations and guidelines covering risk assessment and control of antimicrobial resistance. The group stressed that these should and could only be guidelines since the responsibility for initiating any action would be a matter for national authorities having taken into account all factors involved in order to contain the problem. It was agreed that members of the group would send to WHO draft proposals for such guidelines and that these would then be discussed in the group and with other interested groups.

1.5 The WHONET programme would be amended to take account of comments made by other members of the group so as to make the programme more generally suitable. This amended programme would then form the basis of a pilot project involving initially a few laboratories covering salmonellas isolated from animals and food.

1.6 FEDESA representatives expressed concern about the intended use of the information gathered during the monitoring programme, e.g. whether restriction of the use of an antimicrobial substance would be recommended if certain levels of resistance were detected. There were also questions concerning quality control and on how local - rather than global - problems would be addressed. Despite these reservations, they expressed their support and offered their assistance. The group would welcome information from industry concerning their monitoring programmes and results, details of antibiotic assay methods and of the amounts of antimicrobial substances used.

2. PLANS OF ACTION FOR 1992 - 1993

The group agreed to elaborate a small pilot project on surveillance and assessment of antimicrobial resistance in microorganisms derived from animals, public and environmental health, and clinical medicine by applying the common surveillance methodology outlined in the WHO Guidelines. In this connection the group will continue its activities in 1992/1993 on the following lines:

- the Central Veterinary Laboratory, Weybridge, will collaborate further with the Central Public Health Laboratory, London, in dealing with multisectoral materials and information support;

- data relating to this pilot project would be sought in collaboration with scientists and institutions in the USA, UK, Germany and Japan.

- salmonella derived from affected animals and humans, from the environment (including contaminated feed), from food and other relevant sources, will be examined in the pilot project;

- molecular epidemiology will be studied by conducting plasmid profiles of the microorganisms mentioned above (Berlin Centre);

- computer programmes will be evaluated for data processing and transfer/exchange of data amongst centres involved in the project, in collaboration with Dr O'Brien, Boston, USA;

- the group urged preparation of the draft project document mentioned above, in collaboration with WHO. A proposed document can be found in Annex II.

- draft guidelines on the risk assessment of antimicrobial resistance in health and agriculture will be prepared by October 1992 by Dr Helmuth, Berlin Centre.

- sub-groups will be set up to deal with molecular epidemiology and computer programmes.

- data derived from the pilot project will be analyzed and assessed.

3. CONCLUSIONS AND RECOMMENDATIONS

It was decided to set up a pilot project initially involving the Microbiology Laboratory of the Harvard Medical School, Boston, USA, the CVL in Weybridge, UK, and the Institute of Veterinary Medicine, Berlin. The modified WHONET programme for data entry and exchange will be used for monitoring antimicrobial susceptibility on 500-1000 salmonella isolates derived from animals and feed during the period February-December 1992. The diskettes will be sent to Boston for analysis.

Members of the group were asked to send their proposals for recommendations and for guidelines concerning risk assessment and control of antimicrobial resistance to WHO. When these have been formulated as draft proposals they will be discussed with the group and other interested parties.

Consideration will be given to selectively broadening the membership of the group to reflect the intersectoral nature of the surveillance programme. The group will identify other possible laboratories for further international cooperation and groups engaged in research on enzyme assays and molecular markers will be sought for setting up a sub-group.

The group's activities for implementation of the WHO Guidelines (WHO/Zoonoses/90.167) will be expanded to other regions and interested countries, and the group will provide all possible assistance and support.

ACKNOWLEDGEMENT

The group expressed its appreciation to Dr T.W.A. Little, Director of the Central Veterinary Laboratory, Weybridge, for his hospitality and support during the meeting.

ANNEX I

LIST OF PARTICIPANTS

Dr W.J. Brinley Morgan, 15A Lincoln Drive, Pyrford, Woking, Surrey GU22 8RL, United Kingdom (Chairman)

Dr R. Helmuth, FAO/WHO Collaborating Centre for Research and Training in Food Hygiene and Zoonoses, Institute of Veterinary Medicine (Robert von Ostertag Institute), 88/91 Thielallee, D-W-1000 Berlin 33, Germany

Professor A.H. Linton, Department of Pathology and Microbiology, Medical School, University Walk, Bristol, BS8 1TD, United Kingdom *

Mr I.M. McLaren, Bacteriology Department, Central Veterinary Laboratory, New Haw, Weybridge, Surrey KT15 3NB, United Kingdom

Dr T.F. O'Brien, Director, Microbiology Laboratory, Brigham and Women's Hospital, Harvard Medical School, 75 Francis Street, Boston, MA 02115, USA

Dr B. Rowe, Director, WHO Collaborating Centre for Phage Typing and Resistance of Enterobacteria, Division of Enteric Pathogens, Central Public Health Laboratory, 61 Colindale Avenue, London NW9 5HT, United Kingdom *

Dr C. Wray, Head, Bacteriology Department, Central Veterinary Laboratory, New Haw, Weybridge, Surrey KT15 3NB, United Kingdom (Rapporteur)

Representatives of other organizations

European Federation of Animal Health (FEDESA), Brussels, Belgium:

Dr C. Verschueren, Technical Director
Dr G. Kemp
Dr R. Gustafson
Dr R. Bywater

Secretariat

Dr T. Fujikura, Veterinary Public Health, Division of Communicable Diseases, WHO, Geneva, Switzerland (Secretary)

Dr E.D. Tikhomirov, Microbiology and Immunology Support Services, Division of Communicable Diseases, WHO, Geneva, Switzerland

*Invited but unable to attend.

ANNEX II

Proposed pilot project for surveillance of antimicrobial resistance in clinical medicine, public, animal and environmental health

Background

Antimicrobial resistance can cause serious problems in treating diseases and infections in man and animals. Contamination of food and of the environment by antimicrobial resistant microorganisms has created a pool of donor microorganisms which can then transmit resistance to other microorganisms through mechanisms at the biological, genetical and molecular level.

It has been shown that antimicrobial resistance incidence is closely related to the amount of antimicrobial agents used.

The incidence and patterns of antimicrobial resistance are not always investigated under comparable methods of sampling, testing and interpretation in different laboratories and institutions. Therefore, queries have been raised as to whether such incidences and patterns should become the basis for risk assessment.

The World Health Organization has elaborated Guidelines for Surveillance and Control of Antimicrobial Resistance, indicating procedures and methodologies commonly applied in clinical medicine and public and animal health (document (WHO/Zoonoses/90.167). The WHO working group has agreed to continue collaborative studies, extending their tasks to planning and management of a pilot project for surveillance of antimicrobial resistance in clinical medicine, public and animal health, and the environment; the aim would be to assess the present situation in antimicrobial resistance common to the sectors mentioned above, and to develop measures to mitigate the problems.

1. Long-term objectives

1.1 To survey antimicrobial resistance incidences and patterns in salmonella, E. coli and other microorganisms discussed by the group as indicators, and collected and sampled from various sources such as clinical materials, infected animals, food (including that of animal origin) and the environment. Strains derived from normal materials such as normal flora should also be examined for antimicrobial resistance.

1.2 To examine antimicrobial susceptibility of microbial strains collected using the methods already agreed and elaborated by the group in the WHO Guidelines (WHO/Zoonoses/90.167).

1.3 To interpret the testing results and assess the situation. The group should be re-convened for discussions and further assessment of these results.

1.4 To develop collaborative research on the mechanisms of emergence and occurrence of antimicrobial resistance and of preventive measures in epidemiology, bacteriology, clinical medicine, molecular and biochemical approaches.

2. Immediate objectives

2.1 To collect and examine 500-1000 strains of salmonella from sources in various health and agricultural situations using the methods already agreed and elaborated by the group in the WHO guidelines (WHO/Zoonoses/91.167).

2.2 To conduct the test over a period of 3 to 6 months and to investigate plasmid profiles with special reference to molecular epidemiology.

2.3 To process the resulting data in a computer programme, and to interpret the results and assess the situation, with special reference to risks to the general population.

2.4 To inform those concerned and responsible parties, and publish their report.

2.5 To discuss, plan and implement further steps to be taken.

3. Activities

Dr C. Wray, Central Veterinary Laboratory, Weybridge, UK, will request the collaboration of Dr B. Rowe, Central Public Health Laboratory, London, UK. Plasmid profiles can also be investigated at the Institute of Veterinary Medicine, Berlin, Germany. The data obtained in this collaborative study should be analyzed using a special computer programme (WHONET) by Dr O'Brien, Boston, USA in 1992-1993.

4. Input

US$3000 for the pilot project, using funds from any possible sources.

5. Output

The report of the pilot project should be submitted for publication to the editor of the WHO Bulletin. The group may request any interested institutions and scientists to undertake similar tasks to identify the situation and assess the risks encountered in other areas, countries and regions in order to establish working networks worldwide.

6. Work plans

- February-October 1992: the laboratories mentioned in the three countries named above would test strains. Plasmid profiles of selected strains can be tested at the Berlin Centre.

- August-October 1992: Data processing and analysis by the CVL, Weybridge; the CPHL, London; Dr O'Brien, Boston; and the Centre in Berlin, Germany.

- September-November 1992: Report preparation and publication.

- October/November 1992: Possible working group meeting.

7. Framework

Close and systematic cooperation between the above-mentioned institutions, WHO working group and WHO/VPH-MIM.