

# **Swedish plan of action against antibiotic resistance**

Proposal

The National Board of Health and Welfare, June 2000

## **Summary**

### **Task**

In April 1999 the Swedish Government asked the National Board of Health and Welfare to develop, in collaboration with relevant authorities and organisations, a national plan of action to combat antibiotic resistance. The plan is to encompass all aspects of the resistance problem that have significance for public health, and it is to cover the management within, and effect upon human healthcare, veterinary medicine, animal husbandry and agriculture. The plan of action is limited to antibiotics. **Fotnot:** Antibiotics are naturally-occurring substances that are produced by microorganisms and which inhibit or kill other microorganisms e.g. bacteria. Pharmaceutical agents with antibacterial effects can also be synthesised chemically (antimicrobial agents). Nowadays, the term *antibiotic* also encompasses these chemically synthesised agents with antibacterial properties, but does not include agents against virus or parasite infections, antibacterial substances in disinfectants, other hygiene products or chemical and microbiological biocides.

### **Introduction**

The unrelenting increase in bacterial resistance to antibiotics is posing a threat to the effective treatment of bacterial infections. The pattern of antibiotic resistance remains relatively favourable in Sweden, but significant problems exist even in our country – mainly in hospitals. The international situation is rapidly deteriorating – increasing the risk of imported bacterial resistance. A national plan of action that can outline the necessary measures and identify who must carry them out is therefore urgently needed in order to combat the continuing increase and spread of antibiotic resistance. Antibiotics have uses in many therapeutic areas and all can contribute to the development of resistance. The measures identified in the plan of action extend over many areas and involve many authorities and organisations. The primary aim of this plan of action is to safeguard the availability of effective antibiotic treatment of both humans and animals.

### **Monitoring antibiotic resistance**

Monitoring antibiotic resistance, locally and nationally, is necessary to verify the extent of the problem and to evaluate the effectiveness of any measures taken. On the instruction of the Board of Agriculture, the National Veterinary Institute has begun to monitor resistance in zoonotic and indicator bacteria. The aim is to be able to produce similar information about pathogenic bacteria within three years. In human medicine, the aim is to be able, within a year, to follow long-term trends in antibiotic resistance and to be able to quickly identify the development of serious resistance within healthcare institutions. It is vital that the Institute for Infectious Disease Control initiates and develops a national monitoring service if these aims are to be met.

### **Monitoring antibiotic consumption.**

Sweden has high quality statistics on the sale of antibiotics, but lacks detailed knowledge about treatment indications. A national system for monitoring prescribing indications for antibiotics is a high-priority objective, both in human and veterinary medicine, and ought to be introduced within three years.

### **Measures to prevent infection**

Better compliance with hygiene practices, infection control and vaccination programmes is essential for human and animal health. Reducing infection reduces antibiotic consumption. Specific measures must be taken to limit the problem of resistance in particular environments e.g. in healthcare institutions and nursery schools.

## **Improved diagnosis and antibiotic use**

Guidelines for the diagnosis and treatment of infections and all relevant regulations must be up-to-date, well known and available to all prescribers. Easily accessible and quality assured microbiological diagnostics are important for rational prescribing.

## **Non-medical use of antibiotics**

More information is needed to evaluate the significance of the external environment as a reservoir of antibiotic resistance. The addition of antibiotics to food should be discontinued in favour of other suitable methods. Microorganisms that can spread antibiotic resistance should not be used for plant protection, and alternatives should be found for genetically modified plants that contain marker genes for antibiotic resistance.

## **Drug information and marketing**

The marketing and promotion of antibiotics should not work against the aims of the plan of action. Prescribers of antibiotics should have access to impartial information.

## **Building the knowledge base**

Access to adequate expertise in diagnostics, prevention of infection, antibiotic use and the development of resistance must be surveyed and safeguarded. Continuing education in these areas must be provided for all prescribers and other relevant professionals. Information must be disseminated to the public and high school students. The scientific knowledge base needed to combat antibiotic resistance must be improved.

## **Forms of collaboration and international activity**

An equivalent organisation to the human medical STRAMA needs to be established within veterinary and food sciences, and a plan must be drawn up for the future structure and financing of the work to prevent antibiotic resistance in Sweden. The work that Sweden does in the international arena to combat antibiotic resistance must be properly structured and coordinated and must be based on the current plan of action.

## ***Introduction***

The transformation of antibiotics into effective drugs nearly sixty years ago revolutionised the treatment of infections. Thanks to antibiotics, which have an assured place in today's welfare society, bacterial infections in humans and animals can be cured effectively. This possibility is now under threat as bacteria increasingly develop resistance to antibiotics. There are already today pathogenic bacteria that are resistant to all known antibiotics. Resistance has developed more slowly in Sweden than in many other countries, but resistant bacteria do not respect national borders and have already caused problems for the Swedish healthcare system. If effective countermeasures are adopted, we in Sweden still have a chance of preventing further deterioration that would not only cause greater suffering but also higher drug bills, longer waiting lists and increased mortality.

## **What is antibiotic resistance?**

Antibiotics are substances which act upon microorganisms and inhibit their growth or kill them. They have been used clinically since the end of the 1930s when sulphonamides came into use. The greatest breakthrough was made during the Second World War when penicillin was developed in large scale quantities, and the subsequent years have seen the appearance of a long list of additional antibiotics. When bacteria develop the ability to resist the effects of an antibiotic, this is called "antibiotic resistance". Most of the antibiotics that have been developed for clinical use have been originally isolated from naturally occurring microorganisms (fungi or bacteria). Antibiotics and mechanisms for developing resistance have existed in nature for millions of years, a part of the natural

interaction between microorganisms. For the past 50 years humans have been disrupting this balance by using huge quantities of antibiotics for the treatment of infection in humans and animals and for other purposes, e.g. to promote the growth of livestock or for combating infections in plants. Antibiotic resistance must therefore be viewed in a broad ecological context where resistance can spread between different types of bacteria, between animal species and between different ecological systems. Penicillin-resistant staphylococci were already appearing by the end of the 1940s. Today, resistance has been described against every known antibiotic. It has become increasingly difficult for the pharmaceutical industry to develop new agents.

### **What are the risks of antibiotic resistance?**

Before antibiotics were discovered, the mortality of serious infections, e.g. septicaemia, tuberculosis and pneumonia was extremely high, even in young and previously healthy individuals. Other infections such as tonsillitis, middle ear infections, and urinary tract infections could resolve spontaneously but were often followed by severe and sometimes lethal complications. A reduced availability of effective antibiotics might herald the return of high morbidity and mortality with bacterial infections. Effective antibiotics are also a prerequisite for the prevention and treatment of infections in the context of replacement surgery, e.g. hip joints and heart valves, organ transplantation and cytotoxic therapy for cancer. The consequences of ineffective treatment are, for the patient, increased suffering and delayed or absent response to treatment. The costs of increasing resistance for society as a whole will be enormous, because of longer waiting lists, a greater need for isolation care and increasing drug costs.

#### **Some examples of the consequences of antibiotic resistance**

- ✓ Hospital stays for infections caused by resistant bacteria can be more than double those for infections with susceptible bacteria.
- ✓ The mortality of severe infections in intensive care patients in the USA is over 40% in patients where the first antibiotic introduced is ineffective because of resistance. The mortality in patients infected with bacteria susceptible to antibiotics is less than half this level.
- ✓ The proportion of methicillin resistant staphylococci (MRSA) in septicaemia in England increased from 1.7% in 1990 to 34% in 1998. A similar development in Sweden would result in an extra 40 - 50 million SEK annually in antibiotic costs alone.
- ✓ In Swedish intensive care, up to a quarter of some pathogenic intestinal bacteria are today resistant to ordinary antibiotics, which limits treatment options.
- ✓ Multiresistant tuberculosis is on the increase in many parts of the world. Eastern Europe has one of the highest incidences. The cost of the drugs used to treat just one patient with multiresistant TB is at least 100 000 SEK, whereas the cost of treating infection with normally susceptible TB bacilli is only about 4 000 SEK.
- ✓ The prospects of successful transplantation or cancer treatment are reduced.

### **Which factors influence the spread of antibiotic resistance?**

In Sweden, antibiotics are only used for medical purposes in human and veterinary medicine. In many other countries antibiotics are also used as growth promoters in animal husbandry and as plant protectors. When bacteria come into contact with antibiotics, only susceptible bacteria are inhibited, selecting out resistant varieties and giving them an advantage. All antibiotic use in whatever environment contributes to the

development of resistance and can thereby affect the possibility of finding effective treatment for humans and animals. The relative significance of antibiotic use in different ecological systems is poorly documented. Resistance problems in human healthcare are governed mainly by antibiotic use in humans and is related to extent of use. In addition to the selection of resistant bacteria by antibiotic treatment, spread of infection is encouraged by several other factors, e.g. crowded environments (overcrowded housing, nursery schools, healthcare, residential care of the elderly, animal husbandry) and by poor hygiene.

### **What is the magnitude of the antibiotic resistance problem in Sweden?**

Sweden has, in common with the other Nordic countries, a more favourable pattern of antibiotic resistance than southern Europe and many other parts of the world. The problem of resistance already exists however in Sweden, in both human and veterinary medicine. Within healthcare, this is particularly the case in hospitals, especially intensive care, where antibiotic resistance is increasing in many types of bacteria. The resistance problem is more pronounced in certain parts of the country. As antibiotic resistance can easily spread over national boundaries, we must have mechanisms in place for detecting and preventing further spread of imported resistance.

### **What can be done to reduce the risk of increasing antibiotic resistance?**

The most important principles are those of reducing the need for antibiotic treatment and of avoiding unnecessary use of these agents. This can be achieved by reducing the incidence of infections and by improving knowledge about the correct way to use antibiotics, coupled with efforts to combat the spread of any resistant bacteria that may appear. Antibiotics have many different areas of use, all of which can contribute to the development of resistance. Consequently, countermeasures may involve many different fields of activity. The following plan of action aims to identify what can be considered feasible and reasonably achievable in Sweden over the next few years. A well functioning surveillance system is essential if we are to be able to evaluate the effects of the measures outlined in the plan of action against antibiotic resistance.

### ***The primary aim of the plan of action***

The primary aim of the plan of action is to safeguard the availability of effective antibiotic treatment in both humans and animals.

## **1 Surveillance in human medicine**

### **1.1 Monitoring antibiotic resistance**

Monitoring antibiotic resistance, locally and nationally, is necessary to verify the extent of the problem and to evaluate the effects of any measures taken. It is particularly important to be able to quickly detect the existence of bacteria with serious antibiotic resistance in order to intervene and combat their spread, in healthcare institutions and in society at large. Knowledge of current resistance patterns is also a prerequisite for drawing up new clinical guidelines on antibiotic prescribing. Monitoring antibiotic resistance is based primarily on routine patient investigations carried out in the country's microbiological laboratories, but these must be complemented with targeted investigation of specific issues. Comprehensive resistance monitoring can only be achieved with continuing education and quality control and by collating and analysing locally gathered data at national level.

#### **Aims:**

- To monitor systematically the long-term trends in antibiotic resistance. This aim is to be achieved within a year.
- To detect promptly the occurrence of serious antibiotic resistance in healthcare units and in the community. This aim is to be achieved within a year.

**Activities:**

- The Institute for Infectious Disease Control will be responsible for developing a national programme for the development and registration of standardised methods for the quantitative measurement of antibiotic resistance and for the epidemiological typing of resistant bacterial strains. The county councils will be responsible for ensuring that the programme is supplied with measurement methodologies of adequate quality.
- Systematic sampling according to the programme "Multiresistant bacteria in Swedish Healthcare" will be done on all patients and staff who meet the established risk criteria. Healthcare hygiene experts and local microbiology laboratories will have a special responsibility for seeing that this is done. The Board of Health and Welfare is to assess compliance with this policy within three years.

**1.2 Monitoring antibiotic prescribing**

Sweden has relatively good quality information about the sale and consumption of pharmaceuticals because of the statistics that Apoteket AB make available under an agreement with the state. Information about physician prescribing patterns is however deficient, as is the information about prescribing indications for antibiotics. Several studies in Sweden and abroad have shown that making this type of information available to the prescriber can be an effective way of increasing compliance with current treatment guidelines. It is therefore vital that a system is developed for the continuous monitoring of antibiotic prescribing and treatment indications.

**Aim:**

- To set up a national system for the continuous monitoring and analysis of antibiotic prescribing and its indications within primary and hospital care within three years.

**Activities:**

- The state should continue to guarantee free access to sales and prescription statistics.
- Pertinent authorities and organisations will set up a system for the continuous monitoring and analysis of antibiotic prescribing patterns and indications. Such a system will allow individual prescribers or healthcare units to obtain regular information about their own prescribing patterns and indications in order to make comparisons with other prescribers.
- Pending the development of the above system, STRAMA /Fotnot: STRAMA= The Swedish Strategic Programme for the Rational Use of Antimicrobial Agents and Surveillance of Resistance was established in 1994 and today has representatives from the Swedish Society of Medicine's reference group on antibiotics, the Medical Products Agency, the National Board of Health and Welfare, Apoteket AB, and the Institute for Infectious Disease Control, the Association of County Medical Officers, the NEPI Foundation, the Infection Control Association, the Federation of County Councils, the National Veterinary Institute and the Board of Agriculture. The term STRAMA in this plan of action refers to this network for collaboration between relevant authorities and organisations/ will carry out national surveys of antibiotic prescribing and indications in primary and hospital care.
- The National Board of Health and Welfare together with healthcare authorities will work within the framework of the programme "Healthcare Activity Analysis" (VU 99) so that primary care can regularly obtain overviews of the diagnosis and treatment of infections by extracting information from medical record databases.

- The Institute for Infectious Disease Control and the National Board of Health and Welfare will develop an instrument for the analysis of antibiotic prescribing in relation to community infection patterns.

## 2 Measures to prevent infection

### 2.1 The health of the population

People who are basically healthy are better able to withstand infection. Public health education and preventive healthcare are therefore important. The general standard of hygiene in the community, the food industry and in hospital and local authority care is an important factor that governs the spread of diseases, including those caused by resistant bacteria. Virus infections, e.g. colds and influenza spread easily throughout the community and often pave the way for bacterial infections that require antibiotics. Some environments encourage the spread of microorganisms between individuals. Examples of such environments include nursery schools, healthcare institutions and some forms of residential care for the elderly. These indoor environments hold tightly-knit groups of people with high antibiotic consumption, many of whom have immature or impaired immunity. These places are therefore high risk environments for antibiotic resistance and are discussed separately below.

### 2.2 Vaccinations

The introduction of vaccination during the 20th century has proved to be the most effective medical measure for preventing disease. The disappearance of serious infectious diseases such as tetanus, diphtheria and polio from the public consciousness has led to a certain reduction in the motivation of parents to have their children vaccinated. Clear information is therefore needed to explain why the child vaccination programme remains the basis of good child health. Vaccine safety must be maintained at current high levels. Vaccination of the elderly and of certain risk groups, e.g. patients with cardiovascular disease has played an increasingly important part in reducing the incidence of certain infections, which is why better education is needed to increase uptake.

#### Aims:

- To maintain compliance with the child vaccination programme at 98% or above in the future.
- To gradually increase the uptake of influenza and pneumococcal vaccination to reach a minimum of 60% within 5 years in people over 65 and a minimum of 80% in other medical risk groups.

#### Activities:

- The National Board of Health and Welfare is currently, together with the Medical Products Agency and the Institute for Infectious Disease Control, working on a method for structured national monitoring of child vaccination.
- The National Board of Health and Welfare is currently developing educational material for parents and the general public, and a vaccination handbook for healthcare personnel containing information about the vaccines included in the child vaccination programme.
- The National Board of Health and Welfare will, in collaboration with county medical officers, develop methods for measuring compliance with the vaccination programme for influenza and pneumococci.

### 2.3 Nursery school infections

The body's defence against infection is built up during the first few years of life by contact with various infectious agents. A complex interplay between the individual's immune defence, level of exposure to infectious agents, and a combination of virus and bacteria determines the individual's susceptibility to infectious disease. Many infectious

agents circulate in an environment with many children. Most childhood infections are caused by viruses. These illnesses can be difficult to diagnose and are therefore often treated unnecessarily with antibiotics. Several studies have shown that it is possible to reduce the need for antibiotic treatment by altering hygiene practices at nursery schools. At present, nursery schools lack the structured medical input that could provide advice in the event of e.g. clusters of infection.

**Aim:**

- To reduce antibiotic consumption in children attending nursery school by 20% within three years.

**Activities:**

- The National Board of Health and Welfare is currently working on educational information, which it will later distribute, about infection control measures for nursery schools and methods for evaluating compliance with these.
- County medical officers should act to ensure that consulting physicians are attached to nursery schools.
- A system for documenting sickness absence should be introduced in nursery schools as part of quality assurance.

**2.4 Healthcare-related infections**

The prevalence of antibiotic resistant bacteria is governed by antibiotic consumption and the ability of bacteria to spread through the environment. Healthcare environments are particularly prone to bacterial spread. Antibiotics are used more often here than in other environments and individuals are crowded together. Closer contact between individuals results in increased risk of transmission of bacteria. Patients are also unusually susceptible because of deficient immunity, damaged defence barriers and changes in the normal bacterial flora. Reorganisations in the health service have in many instances led to reduced floor space per patient, more patients per carer, a higher proportion of severely ill patients, greater mobility of patients between different care levels and reduced possibilities for nursing in individual rooms. This has contributed to an increased risk for spread of infection. A plan of action for combating the development of resistance must include measures that deter the spread of bacteria in general and of antibiotic resistant bacteria in particular, both in hospitals and in local authority residential and nursing homes.

**Aims:**

- To stop the spread of multiresistant bacteria from known or strongly suspected sources of infection within the healthcare system, residential homes, domiciliary care, or with the transfer of patients between such environments. The aim should be achieved within a year.
- To introduce a system for monitoring healthcare-related infections as a part of continuous quality control. This aim should be achieved within five years.

**Activities:**

- The national programme for combating the spread of multiresistant bacteria is to be publicised and used by all healthcare personnel. County councils, with their hygiene expertise, and regional STRAMA groups have a particular responsibility for implementing the programme.
- The need for individual rooms is to be highlighted during the planning of wards and intensive care units.

- Healthcare hygiene expertise is to be made available wherever healthcare is being provided.
- Every carer, aided by hygiene experts, is to help to establish systems for monitoring healthcare related infections.
- County councils and other healthcare providers are to work to establish best practices for information transfer on planned transfer of patients between healthcare units.

### 3 Improved diagnosis and antibiotic use

As antibiotics are only active against bacteria, it is important to distinguish between viral and bacterial infection. Good diagnostic practices improve the chances of avoiding unnecessary antibiotic treatment. More than 90% of antibiotic prescriptions are issued to patients being cared for outside hospitals, mainly children and the elderly. Even if hospitals only account for a small part of total antibiotic consumption, the number of patients treated concurrently in a confined space represents a big risk for the appearance and spread of resistant bacteria. This also applies to nursery schools and care institutions. A delay in providing effective treatment can lead to complications and, in serious infections, to increased mortality. The rise in antibiotic resistance makes it all the more important to identify bacteria and their resistance patterns as quickly as possible. In order to introduce effective treatment before bacteria have been isolated, it is important that the microbiology laboratory provides the prescriber with guidance on antibiotic susceptibility and that up-to-date guidelines are available.

#### **Aims:**

- To formulate local guidelines within three years for the diagnosis and treatment of bacterial infections based on national and regional guidelines.
- To ensure that prescribers of antibiotics are familiar with and follow current guidelines. This aim should be achieved within three years.
- To ensure that all microbiological diagnostic procedures are quality-controlled and that preliminary results of routine cultures are normally obtainable within one day. This aim should be achieved within a year.

#### **Activities:**

- The scientific basis for guidelines on diagnosis and treatment of infections in primary care and hospitals should be agreed nationally, preferably coordinated within the framework of STRAMA. The guidelines could be complemented by local recommendations and should be made easily available at every unit where these diseases are common.
- Every hospital-based unit where antibiotics are used should have infectious disease expertise at hand.
- Local diagnosis-related prescribing patterns and compliance with treatment guidelines should be monitored and analysed. Every primary care area should appoint a doctor with special responsibility for liaison, evaluation and continuing education in the field of antibiotics.
- Local written instructions that include regular follow-up of methodological reliability should be applied to decentralised laboratory diagnosis of infections. The National Board of Health and Welfare and the Institute for Infectious Disease Control are to gather the knowledge and data on which the evaluation of diagnostic methods, particularly in primary/outpatient care, can be based.

## 4 Surveillance

### **4.1 Monitoring antibiotic resistance in bacteria from animals**

The effectiveness of a plan of action against antibiotic resistance can only be assessed with continuous information about resistance patterns. The development of resistance

ought to be followed closely and undesirable changes detected promptly. The results should be reported and analysed against the background of antibiotic consumption and disease patterns. Methods of reporting and analysis should maintain a high standard and the results should be expressed in a form that allows comparison with those of other countries. In 1999 the National Veterinary Institute began to monitor the resistance patterns of zoonotic and indicator bacteria on the instruction of the Board of Agriculture.

**Aim:**

- To monitor continuously in future the resistance patterns of zoonotic and indicator bacteria, and to begin to collect equivalent information about resistance in essentially pathogenic animal bacteria within three years. It should be possible to compare the results of resistance monitoring programmes of different member states of the EU within five years.

**Activities:**

- The National Veterinary Institute will be responsible for the reporting and analysis of relevant statistics.
- All pertinent authorities will work within networks, reference groups and committees to ensure that the programme for monitoring resistance is extended to the EU according to established minimum criteria.

**4.2 Monitoring antibiotic resistance from food**

Food is the principal route for the spread of resistance between animals and humans. Little is known at present about the prevalence of resistant bacteria in food.

**Aim:**

- To establish a working system for monitoring of resistance in zoonotic and indicator bacteria in food within three years.

**Activities:**

- The National Food Administration should, in consultation with the National Veterinary Institute and STRAMA VL, **/Fotnot:** STRAMA VL is an organisation for coordinating activities in veterinary medicine and the food industry as suggested in chapter 10/be given the task of planning, implementing and reporting a programme for resistance monitoring within three years.

**4.3 Monitoring antibiotic prescribing**

The total sales of antibiotics for use in animals have been registered by Apoteket AB since 1980. An accounting system should however also present the results according to diagnosis, prescriber and type of animal. In 1999, the Board of Agriculture, on the instruction of the Ministry of Agriculture, Food and Fisheries, therefore produced a proposal for a system that could record the necessary information.

**Aim:**

- To implement a system within three years for presenting annual information about the prescribing of antibiotics to animals in the food chain according to type of animal. It should also be possible to register diagnosis and prescriber. It should be possible to implement a similar system for sporting animals and household pets within five years.

**Activities:**

- The Board of Agriculture will be responsible for achieving this aim, in consultation with a reference group, e.g. STRAMA VL.

## 5 Measure to prevent infection in veterinary medicine

Antibiotics may be prescribed for infections irrespective of whether they are caused by viruses, bacteria, parasites or any combination of these microorganisms. A general reduction in the spread of infections reduces the need for antibiotics and delays the appearance of bacterial resistance. Deficiencies in the environment, feeding practices and husbandry makes animals more susceptible to infections and are an important factor in the incidence of disease. Measures to prevent disease include hygiene, animal welfare, biosecurity and in some cases vaccination. Carefully planned husbandry and feeding is also very important. Disease prevention, advisory services and voluntary surveillance programmes have been set up for different types of animals by organisations such as the Swedish Fish Health Control Programme, the Swedish Animal Health Service, the Swedish Meat Poultry Association, the Swedish Dairy Association and the Swedish Egg Producers Association. This work is carried out in close collaboration with relevant authorities, when pertinent.

### 5.1 Animal diseases that occur in Sweden

#### 5.1.1 Ruminants and swine

Three disease categories in food production animals account for the greater part of antibiotic use in Swedish veterinary medicine. These are mastitis in milking cows together with diarrhoeal illnesses and respiratory infections in pigs and cattle. Every year nearly a fifth of the country's milking cows are treated for mastitis. Diagnosis is vital for targeted treatment. Mastitis can even occur in the absence of any obvious signs of illness. At present, we do not know to what extent this latter category is treated with antibiotics.

An extra effort must be made to prevent diarrhoea and respiratory infections in growing pigs and cattle. Infection with bovine viral diarrhoea virus is an important cause of illness in cattle. A state-sponsored and subsidised voluntary control programme for this viral infection has been operational in Sweden since 1994. The programme has been greatly appreciated by farmers, and over 28 000 herds are enlisted of which over 19 000 have been declared free from infection.

#### Aims:

- To reduce the incidence of mastitis in milking cows by 20% within five years.
- To reduce the number of pig and cattle herds needing repeated treatment for diarrhoeal or respiratory infections by at least one third within five years.
- To eradicate bovine viral diarrhoea virus from Sweden within five years.

#### Activities:

- The Board of Agriculture's system for measuring the incidence of disease and treatment will be reviewed as regards the above disease categories. STRAMA VL will analyse the statistics every year and suggest measures where necessary.
- An education programme centred upon the best available techniques and methods for treating and preventing mastitis and aimed at the various relevant parties **ought** to be formulated and introduced by STRAMA VL in collaboration with relevant organisations.
- The National Veterinary Institute and the Board of Agriculture are to survey current guidelines regarding the treatment of subclinical mastitis.
- The Board of Agriculture and The National Veterinary Institute will develop, in collaboration with STRAMA VL, a programme for promoting measures against diarrhoeal and respiratory infections in growing pigs and cattle.

- The Board of Agriculture will implement an obligatory programme to combat bovine viral diarrhoea virus.

### **5.1.2 Poultry**

The bacterial intestinal illness necrotising enteritis is prevented today with a combination of poultry management and feeding measures together with the use of anti-parasitic agents. A voluntary control programme run by the producer organisation aims to develop a form of poultry management that protects against illness without the need for regular medication. Other bacterial poultry infections that require antibiotic treatment rarely occur in Sweden.

#### **Aims:**

- To replace the use of antibiotics for the prevention of parasitic and bacterial intestinal disorders in chickens with other methods within ten years.
- To hold the future proportion of meat poultry flocks suffering outbreaks of infectious illnesses that require treatment to current levels.

#### **Activities:**

- The National Veterinary Institute should develop and evaluate methods for preventing bacterial intestinal disturbances in chickens, in consultation with producer organisations.
- The Board of Agriculture is to keep annual statistics regarding antibiotic consumption linked to diagnosis in poultry, mainly meat poultry. The statistics should be continually analysed by STRAMA VL who should suggest measures as necessary.

### **5.1.3 Fish**

Antibiotics may be required to treat up to ten types of infection in farmed fish. There are effective vaccines against some of these infections. Increasing vaccination of fish between 1997 and 1999 has markedly reduced the need for antibiotics for these indications. It is nowadays rare for treatment to be given to fish meant for consumption.

#### **Aim:**

- To maintain the incidence of infections requiring antibiotics in farmed fish at current levels.

#### **Activity:**

- The Board of Agriculture should work with producers to achieve this aim.

### **5.1.4 Sporting animals and household pets**

Several infections in sporting animals and household pets can be prevented by vaccination. These include equine influenza, which is endemic throughout the country. This infection is easily spread as horses are often transported for competitions, training and sale, and infection can lead to complications that require antibiotic treatment. At present, opinions are divided about the need for vaccination of competition horses.

#### **Aim:**

- To achieve high compliance with recommended vaccination programmes.

#### **Activities:**

- The National Veterinary Institute and the Board of Agriculture will work, in consultation with representative organisations, on a programme to inform about, and encourage the adoption of correct vaccination practices against relevant infections.
- The Board of Agriculture and The National Veterinary Institute will continuously monitor the level of compliance with current recommendations.

### **5.2 Animal illnesses that do not normally occur in Sweden**

Sweden's animals are free from all infections that the Office International des Epizooties (OIE) considers to have the greatest socio-economic significance. The reasons for this include Sweden's peripheral location, sparse animal population, tradition of combating and eradicating disease and strict import restrictions for animals. Membership of the EU means that Sweden can no longer enforce the same import restrictions. Sweden has applied for special rules in regard to approximately twenty diseases. As the European Commission has yet to consider these applications, Sweden still applies quarantine on importation. At the same time, voluntary surveillance organisations have been formed by the farming industry. These apply import rules that ensure that the pattern of disease that preceded membership is maintained.

#### **Aim:**

- To ensure that no infectious disease new to Sweden and listed on the OIE's A or B list is allowed to establish itself in Swedish pets.

#### **Activities:**

- The Board of Agriculture is responsible for seeing that current regulations are applied, ensuring that the importation of foreign infectious agents is prevented as effectively as possible.
- The Board of Agriculture, in collaboration with the National Veterinary Institute, will encourage voluntary undertakings by interested organisations as regards the biosecurity of animal importation.

### **5.3 Zoonoses**

Zoonoses are diseases that can be transmitted between animals and humans. The commonest food-borne zoonosis in Sweden is campylobacter infection. The number of human cases is on the increase and 6 544 cases were reported in 1998, about half of which were contracted within Sweden. Larger outbreaks are often related to unpasteurised milk or to drinking water. Occasionally, chicken has been identified as the dominant source of infection. Over the past ten years the poultry industry has taken measures to dramatically reduce the incidence of campylobacter in chicken flocks. A corresponding reduction in the incidence of human infection has not been seen, making it necessary to search for other sources of infection.

Only one in ten people that contract salmonella have been infected in Sweden. In 1998, not a single case could be traced to domestically produced animal food products, which indicates that the national control programme works well. The term domestically produced includes both food produced in Sweden and food prepared in Sweden from imported produce. It remains unclear how and by whom suspected salmonella infection transmitted from pets to humans should be investigated. Particular attention must be paid to the appearance of multiresistant salmonella which is an increasing problem in other countries.

#### **Aims:**

- To reduce the annual rate of human campylobacter infection contracted domestically to 50% of the 1999 level within ten years.

- To maintain the annual incidence of human salmonella infection contracted domestically at today's low level.
- To prevent the spread of multiresistant salmonella to animals in the Swedish food chain.

**Activities:**

- The Zoonosis Centre will initiate the development of methods of tracing infection and documenting sources of human campylobacter infection.
- The Zoonosis Centre will evaluate salmonella controls, in collaboration with other Nordic countries.
- The Zoonosis Centre will formulate recommendations for measures to be taken in response to the detection of multiresistant salmonella and in response to the detection of salmonella in sporting animals and household pets.
- The Institute for Infectious Disease Control, local authorities and county medical officers are to account annually to the Zoonosis Committee for epidemiological investigations performed and disease control measures taken in documented cases of zoonotic infection.
- The Board of Agriculture will be responsible for the maintenance of salmonella surveillance and its extension into animal husbandry and the handling of animal feed.

## 6 Improved diagnostics and use of antibiotics

Microbiological diagnostics must be readily available, reliable and used correctly if antibiotics are to be used to good effect. Guidelines on good veterinary practice regarding use of diagnostics and choice of therapy are needed as a resource during the ordinary working day. The Swedish Society of Veterinary Medicine is currently working on animal-specific treatment guidelines.

The National Board of Agriculture's pronouncement (LSFS 1979:8) regulates the prescribing and dispensing of veterinary drugs and the ordering of medicated feed for animals. It imposes restrictions on prescribing but is out of date in some respects. The application of current rules and regulations must be monitored and deficiencies corrected. Individual veterinary surgeons should have access to their own prescribing statistics.

**Aims:**

- To further develop species-specific guidelines on good veterinary practice in the diagnosis and treatment of infections, and to see that these guidelines are made available and put into practice within four years.
- To update current regulations so that they too in future lend support to the aims of the plan of action, and to put in place a system for monitoring veterinary antibiotic prescribing within three years at the latest.
- To make laboratory diagnostics and autopsy services available throughout the country.

**Activities:**

- The National Veterinary Institute will work in collaboration with The Swedish Society of Veterinary Medicine and STRAMA VL to produce guidelines on good veterinary practice in the diagnosis and treatment of infections.
- The Board of Agriculture is to review the need for, and availability of regional laboratory and autopsy services throughout the country.
- All clinical microbiological diagnostics at veterinary laboratories are to be accredited.
- The National Veterinary Institute will review documentation related to relevant tests used in the field.

- The Board of Agriculture will amend its pronouncement LSFS 1979:8 so that the statutes are clarified and harmonised with other legislation, and will devise and apply a system for registering the antibiotic prescribing of individual veterinary surgeons.

## 7 Non-medical use of antibiotics

### 7.1 The ecological effects of antibiotics

Both antibiotics and antibiotic resistant bacteria can reach the wider environment in sewage and manure, becoming a reservoir of antibiotic resistance. Lack of knowledge in this area means that we are unable to quantify the risks that this entails. As both antibiotic use and resistance are increasing, we need to establish the facts so that we can decide if measures are needed to limit risk.

#### **Aim:**

- To produce, within five years, a factual basis for the evaluation of possible risk to humans and animals associated with the release of antibiotics and resistant bacteria into the environment.

#### **Activities:**

- The Swedish Environmental Protection Agency should be given the task of establishing how much of the various types of antibiotics is released into the environment annually, as well as their pathways and final destinations.
- The Swedish Environmental Protection Agency should be given the task of establishing, in collaboration with the Medical Products Agency, how the various classes of antibiotics are broken down in different environments.
- The Institute for Infectious Disease Control and the National Veterinary Institute will establish the extent to which resistant bacteria in the environment survive, spread and reinfect humans and animals.

### 7.2 Antibiotics in food

At present, two antibiotics - nisin and natamycin - are approved as food additives within the EU. These substances may be used to prevent the growth of certain bacteria and moulds in dairy and meat products. Nisin is produced by lactic acid bacteria and therefore occurs naturally in some fermented foods. It is not used as an antibiotic these days but it has antibacterial activity and has lately received attention as a possible candidate for development into a pharmaceutical. Natamycin is active against fungi and can be used for local treatment of fungal infections.

#### **Aim:**

- To replace the addition of antibiotics to food by other approved methods within five years.

#### **Activities:**

- The National Food Administration is to document the occurrence of antibiotic additives in food currently sold for consumption in Sweden, as well as evaluate any benefit that these substances and their possible alternatives might provide.
- The National Food Administration should consult with other relevant authorities in EU issues pertaining to antibiotic food additives.
- Sweden should also work to achieve these aims within the EU.

### **7.3 Antibiotics as plant protectors**

No plant protectors containing antibiotics may be used in Sweden. On the other hand, preparations that contain microorganisms that naturally produce antibiotic substances are used. Antibiotics are used directly on crops in other EU countries.

#### **Aims:**

- To stop the use within the EU of microorganisms for crop protection when this can promote the spread of antibiotic resistance.
- To replace within six years antibiotics that may have or acquire significance for human or veterinary medicine with other approved alternatives for the purpose of plant protection in the EU.

#### **Activities:**

- Sweden continues to work for the achievement of these aims in the EU.
- The Swedish Chemicals Inspectorate shall, in consultation with other relevant authorities, monitor and work to prevent the approval of plant protectors that can lead to the spread of antibiotic resistance.

### **7.4 Antibiotic resistance in genetically modified organisms (GMO)**

Genetically modified organisms (GMO) are organisms, e.g. plants and microorganisms, that have had their inherited properties altered by genetic techniques. When GMO are created, a selective marker gene is usually attached to the introduced foreign gene. With the aid of the marker gene it is then possible to select out those cells that have taken up the introduced gene. Antibiotic resistance genes are often used as selective marker genes. The relevant Swedish authorities consider that the risks of using genes for antibiotic resistance as markers in genetically modified plants are very small. The risks of using marker genes that can introduce antibiotic resistance into genetically modified microorganisms (GMM) is considered to be greater, as microorganisms can naturally exchange genetic material. When GMM with antibiotic resistance genes are deliberately released into the environment, or are accidentally released from sealed areas, e.g. laboratories, there is a risk of spreading resistance to other microorganisms in the environment.

#### **Aims:**

- To replace the use of antibiotic resistance marker genes in genetic modification of plants destined to be released into the environment with safe alternative techniques within five years.
- To confine genetically modified microorganisms possessing acquired antibiotic resistance to the laboratory environment.

#### **Activities:**

- The Swedish Chemicals Inspectorate and the Board of Agriculture will work to ensure that antibiotic resistance genes are not used in genetically modified plants and that plants that contain such genes are gradually removed from the market.
- The Swedish Work Environment Authority will monitor regulatory compliance during this type of laboratory work.

## **8 Drug information and marketing**

It is vital that prescribers of antibiotics have easily accessible, up-to-date, impartial, scientific information about antibiotics that is compatible with Swedish guidelines for

antibiotic prescribing. The Medical Products Agency produces information about newly-registered drugs in the form of product monographs. Corresponding information is not available for drugs that have been on the market for a long time. In human medicine, local pharmaceutical committees and regional STRAMA groups play an important role in providing prescribers with objective drug information and therapeutic guidelines. A continuous dialogue between the various parties can identify problems and clarify restrictions, promoting rational marketing.

**Aims:**

- To ensure that antibiotic information and marketing does not run counter to the aims of the plan of action.
- To ensure that easily accessible and non-commercial information becomes an important source of knowledge for antibiotic prescribers.

**Activities:**

- Non-commercial information concerning antibiotics should be produced through better cooperation between the Medical Products Agency, local pharmaceutical committees, RAF (the Swedish Society of Medicine's Reference Group on Antibiotics), Apoteket AB and the National Veterinary Institute and could be disseminated via STRAMA/STRAMA VL.
- Better collaborative channels will be developed between the Swedish Association of the Pharmaceutical Industry and STRAMA/STRAMA VL.

## 9 Building a knowledge base

### 9.1 Education

The success of the plan of action requires that all personnel in healthcare, animal healthcare, animal husbandry and food production apply current knowledge and best practices. Prescribers of antibiotics must have an adequate knowledge base for deciding whether or not to prescribe antibiotic treatment and to be able to make a rational therapeutic choice. All personnel must know how infections can be prevented. Antibiotics and antibiotic resistance are dynamic subjects, which means that knowledge must be continually updated. It is something of a problem that the shortage of knowledgeable experts in the field makes it difficult to reach a wider audience.

**Aim:**

- To ensure that prescribers and other relevant personnel have adequate and up-to-date knowledge about the prevention and diagnosis of infection, antibiotic use and development of resistance.

**Activities:**

- The Board of Health and Welfare and the Board of Agriculture will work on plans to ensure that the availability of competent educators is sufficient to achieve the above aim.
- The authorities responsible for all basic and further education involving human and veterinary medicine will review and evaluate course content in relation to the above aim and upgrade content to the necessary extent.
- All employers in human and veterinary healthcare and in food handling will formulate a plan for continuing skills development and evaluation in the areas mentioned in the above aim.
- The Board of Health and Welfare and the Board of Agriculture will be responsible for the development and implementation of methods for monitoring the knowledge and attitudes of relevant personnel categories.

## 9.2 Information

A reduction in the spread of infections requires that the general public has a good understanding of the importance of personal and food hygiene. In addition, an understanding of the risks and benefits of antibiotics is needed. Information provided by relevant authorities can be disseminated by schools, pharmacies, consumer organisations etc.

### Aim:

- To ensure that within three years at least 50% of the population is aware of the problem of antibiotic resistance and its causes.

### Activity:

- Relevant authorities will prepare educational material and basic information about antibiotics and resistance.

## 9.3 Research

Research into antibiotics has hitherto been largely financed by the pharmaceutical industry and has almost exclusively been focused on the development of new drugs. Little public money has been spent on other antibiotic research with the consequence that there are gaps in our knowledge about the development of resistance. Another important factor has been the tendency to focus on the problems of the individual patient. The strategies that have been developed to combat the development of resistance at community level have therefore been largely based upon historical experience rather than scientific documentation. A knowledge base of higher quality would enable more effective strategies, which is why research critical to the subject must be given high priority. Research must be coordinated internationally if scientific benefits are to be maximised.

### Aim:

- To improve substantially the scientific knowledge base needed to combat antibiotic resistance within five years at the latest.

### Activities:

- Relevant authorities will arrange, in consultation with research committees and other funding bodies regular meetings about antibiotic resistance in order to chart the progress of research and to obtain a basis for future priority decisions.
- Relevant research committees, strategic funds and foundations **should** formulate and implement a plan for stimulating high quality Swedish research and collaborative international research into resistance epidemiology, infection control and other priority issues.

## 10 Forms of collaboration and international efforts

### 10.1 The future shape of organisation and collaboration

A close collaboration between all sectors - public, charitable, and commercial organisations is of great importance for achieving the aims of the plan of action. It is important that the media, the public and all that come into professional contact with antibiotic treatment are provided with consistent information about how authorities and experts see the situation and which measures must be taken. In 1994 a collaborative body in the field of human medicine was formed. STRAMA (The Swedish Strategic Programme for the Rational Use of Antimicrobial Agents and Surveillance of Resistance) has fulfilled this function and received financial support in 2000 for a maximum of 3 years via the Dagmar agreement. A corresponding body, STRAMA VL, ought to be

created to meet similar needs in the fields of veterinary medicine and food production. STRAMA VL ought to be independent but can be linked organisationally to the National Veterinary Institute.

**Aims:**

- The plan of action shall be continuously reviewed and updated, and a biennial report is to be given to the Government.
- The organisational structure of the national effort to achieve the aims of the plan of action ought to be established within two years.

**Methods:**

- The Ministry of Agriculture Food and Fisheries should be given the task of establishing an independent organisation for collaboration across sector boundaries (STRAMA VL) on issues aimed at combating antibiotic resistance, and for which it ought to establish an administrative office.
- The Ministry of Health and Social Affairs and the Ministry of Agriculture Food and Fisheries are to formulate a plan for the future organisation and financing of STRAMA and STRAMA VL.
- The Board of Health and Welfare should be given the task of coordinating the follow-up of the plan of action and of updating the aims as necessary.
- The Board of Health and Welfare should be given the task of providing reports to the government.

**10.2 International efforts**

The antibiotic resistance situation in Sweden is affected not only by how we act domestically. Open borders with increasing trade and communication are accompanied by risks of importing new problems. The Swedish state, together with private and charitable organisations, is today working internationally in various forums and at various levels for a greater common vision and better exchange of information about current issues. An effective plan of action against antibiotic resistance demands that work on resistance monitoring programmes, prescribing statistics, issues of infectious disease control including food issues, and on promoting public health driven systems of animal husbandry is given high priority. It is vital that all such work is based on sound science and is well coordinated.

**Aims:**

- To obtain international acceptance for the aims of the Swedish plan of action.

**Methods:**

- The Swedish Government should work internationally to combat antibiotic resistance, using the plan of action as a platform.