The World Health Assembly (WHA) adopted a resolution in May, 2014 that has urged member countries to take urgent action on the cause of antimicrobial resistance (AMR). The Director-General, World Health Organisation (WHO) is to develop a draft global plan that is to be presented at the WHA 2015 for approval. Earlier in April, 2014, the WHO released its first global surveillance report on antimicrobial resistance. Though it has been trying to address the cause of AMR since 2001, but only after a decade came up with a policy package for member countries stressing on surveillance of AMR and regulatory framework to control antibiotic use in food-producing animals. A list of critically important antibiotics that need to be preserved for human medicine has also been developed.

In 2010, the WHO entered into a tripartite agreement with Food and Agricultural Organization (FAO) and the World Organization for Animal Health (OIE). The ‘One Health’ approach is aimed for joint action to enhance global coordination and promote inter-sectoral collaboration between public health and animal health sectors as well as in food safety. OIE has also published guidelines for national antimicrobial surveillance programs in animals and for responsible use of antimicrobials in them.

COUNTRY-LEVEL INITIATIVES AND IMPACT

Some of the European countries banned penicillin, streptomycin, and tetracyclines as antibiotic growth promoters (AGPs) in 1970s. Later in 1986, Sweden banned all AGPs in food-producing animals, which was followed by Denmark. The European Union (EU) was influenced by evidence in Denmark and prohibited all AGPs in 2006.

Broadly, the regulatory initiatives across several countries involve:
- Prohibiting (see Table 1) AGPs and antibiotics that are critical for human use
- Creating infrastructure to monitor resistance in human, food-producing animals and in food chain (see Table 2)
- Increased supervision on antibiotic prescriptions by veterinarians and its use by farmers

Table 1: Timeline of ban on antibiotic growth promoters

<table>
<thead>
<tr>
<th>Country/ Union</th>
<th>Banned antibiotic</th>
<th>Year of banning</th>
</tr>
</thead>
<tbody>
<tr>
<td>Some European countries</td>
<td>Tetracycline, penicillin, streptomycin</td>
<td>1972-74</td>
</tr>
<tr>
<td>Sweden</td>
<td>Antibiotic use as growth promoter</td>
<td>1986</td>
</tr>
<tr>
<td>Denmark</td>
<td>Avoparcin</td>
<td>1995</td>
</tr>
<tr>
<td>EU</td>
<td>Avoparcin</td>
<td>1997</td>
</tr>
<tr>
<td>Denmark</td>
<td>Virginamycin</td>
<td>1998</td>
</tr>
<tr>
<td>Denmark</td>
<td>Tylosin, spiramycin, zinc bacitracin</td>
<td>1998</td>
</tr>
<tr>
<td>EU</td>
<td>Virginamycin, tylosin, spiramycin, zinc bacitracin</td>
<td>1998</td>
</tr>
<tr>
<td>EU</td>
<td>Antibiotic use as growth promoter</td>
<td>2006</td>
</tr>
<tr>
<td>Netherlands</td>
<td>Antibiotic use as growth promoter</td>
<td>2006</td>
</tr>
</tbody>
</table>

Source: Danish Veterinary and Food Administration: Fact sheets on the Danish restrictions on non-therapeutical use of antibiotics for growth promotion and its consequences; European Commission: Ban on antibiotics as growth promoters in animal feed enters into effect; Feedstuffs Act, Sweden 1985; Government of the Netherlands: Reduced and Responsible, Policy on the use of antibiotics in food-producing animals in the Netherlands.
Largely, the impact observed includes reduction in antibiotic usage particularly of AGPs with no negative effect on productivity and decreasing resistance in some cases. However, the US continues to follow a voluntary approach which is less effective than regulations followed in the EU.

### EUROPEAN UNION

After a series of prohibitions on individual AGPs since 1997-98, the EU banned all AGPs in 2006. AMR has been monitored since 2000 by the European Antimicrobial Resistance Surveillance Network (EARS-Net). Antimicrobial usage in humans and in animals is recorded by the European Surveillance of Antimicrobial Consumption (ESAC) and European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) respectively. Aiming to combat resistance, the European Commission (EC) issued an action plan in 2011 suggesting the responsible use of antibiotics in both animals and humans; promoting development of new antibiotic; improving surveillance; preventing microbial infections, their spread and to contain the risks of AMR.

Use of AGPs has been reduced in several countries such as Denmark, Netherlands and Sweden.

### DENMARK – A CASE STUDY

Denmark is a major livestock producer in Europe and is the largest exporter of pork in the world. It produces pigs much more than other livestock or poultry. About 80 percent of animal antibiotic use is for pig production. It is one of the leading countries in regulating antibiotic use since early 1990s.

Initiative: Ban on antibiotics: In order to decrease the animal reservoir of resistant bacteria, which posed a potential risk to public health, Denmark banned the use of AGPs in food-producing animals. In 1995, a study on chicken that linked avoparcin use for growth promotion and presence of vancomycin resistant bacteria led to the ban of avoparcin. Subsequently, in 1998, virginiamycin, tylosin, spiramycin and zinc bacitracin were banned as growth promoters. Later in 2002, fluoroquinolones were allowed only if no other antibiotics could be used as per laboratory test for that disease and animal. In terms of voluntary initiatives, the cattle and broiler industry, voluntarily stopped use of all AGPs in 1998 and the swine industry followed it in 2000. In 2010, the swine industry stopped all use of cephalosporins.

Regulating veterinary practice: In 1994-95, the prophylactic use of antimicrobials was prohibited and the veterinarians’ profits from direct sales of medicine were fixed at a maximum of 10%. As part of the voluntary ‘herd health contracts’, monthly farm visits of veterinarians were promoted to optimise antibiotic use. In 2000, VetStat was established that recorded every antibiotic prescribed to food-
producing animals. In 2005 and later in 2007, action plans were introduced for reduction and prudent use of antimicrobials, which included treatment guidelines for veterinarians, audit and supervision of veterinarians. 18 It also aimed to ensure that there is no economic relationship between veterinarians and pharmaceutical industry.

Later in 2010, a ‘yellow card’ initiative, was adopted by the Danish Veterinary and Food Administration (DVFA) to set threshold levels for antibiotic consumption in pigs. 19 If a farm holding pigs exceeds threshold levels, the DVFA may issue an order or an injunction (yellow card) to reduce antibiotic consumption within nine months. If the order is not complied with, the DVFA may issue further injunctions.

Resistance monitoring: In 1995, a comprehensive surveillance program – Danish Integrated Antimicrobial Resistance Monitoring and Research Programme (DANMAP) – was initiated to monitor resistance trends in meat, live food-producing animal and human. DANMAP reports annually.

IMPACT

- Swine production has grown with similar rates before and after the ban of growth promoters. It has increased by 47 percent between 1992 and 2008, while the antimicrobial use got reduced by 51 percent from 100.4 to 48.9 mg/kg meat. This is much lower than in the US. 20
- Since 1995, production in poultry has increased to some extent but there has been about 90 percent reduction in total antimicrobial use in 2008. From about 5,000 kg it has dropped to about 500 kg that is used for treatment of sick birds only. 21
- In broilers, productivity (measured as kg of broilers per square meter) and mortality was not affected by the termination of growth promoters. The feed conversion ratio increased, but the amount spent on feed was gained again as there were no expenses on growth promoters. 22
- Estimated in 2003, there was no net rise in cost of poultry production. Just over one percent increase (about EUR 1) was estimated in case of pigs. 23
- Antibiotic resistance significantly decreased in pigs and broilers from 1996 to 2008. Avoparcin and virginiamycin resistant E. faecium from broilers and pigs reduced after ban on avoparcin and virginiamycin respectively. Similarly, macrolide resistance (due to tylosin) and avilamycin resistance got decreased in E. faecium among broilers. 24 See Fig. 1 for details on the impact.

NETHERLANDS

Initiative: Netherlands phased-out the use of AGPs in 2006 along with the EU, but the therapeutic use for antibiotics was high and rising. During 2008-11, a policy – as a public-private partnership – for a substantial reduction and more responsible use of antibiotics in the livestock industry was drafted. This happened due to public concerns about transfer of antimicrobial resistance from livestock to humans. Its key elements were transparency and benchmarking of antibiotic use per herd and per veterinarian; improvement of herd health with clear responsibilities for farmer and veterinarian; and antibiotic reduction targets for livestock production as a whole: -20% in 2011 and -50% in 2013 with reference to the amount sold in 2009. 25

In 2011, with the recommendations of the Health Council of the Netherlands, human healthcare risks became pivotal for Dutch antibiotics policy in livestock production. The recommendations include, shift in the focus to Extended-Spectrum Beta-Lactamases (ESBL)-related risks, substantial reduction in 3rd and 4th generation cephalosporins, ban on systematic use of beta-lactam antibiotics, fluoroquinolones and aminoglycosides. 26 Other recent rules in Netherlands include that farmers must register all antibiotic use, so that it is possible to see how many antibiotics their livestock receives on an average; a penalty can be imposed on farmers who deliver animals for slaughter which contain high levels of antibiotic residues; ‘Last-resort’ antibiotics for humans may only be administered to sick livestock as a last resort; the raw materials for veterinary medicinal products may not be sold without a licence; and pet stores may not sell antibiotics.
FOOD SAFETY

Since March 2014, veterinarians can prescribe antibiotics only after they have conducted a clinical inspection and made a diagnosis. The entire regimen of antibiotics must then be administered by the veterinarian. Antibiotics may not be stored on-site at the farm.

Impact: The policies initiated in 2008 to limit antibiotic usage were highly successful. In 2012, nearly 50 percent reduction (249 tonnes) in antibiotic use for food-producing animals was observed since 2014.
2009, when it was 495 tonnes. It aims to reduce further 20 percent by 2015. The use of antibiotics which are critical to humans have been reduced to a minimum. In 2012, the resistance levels in indicator organisms from all animals have decreased including the occurrence of cefotaxime resistance in *E. coli* from broilers, which clearly decreased after the ban of cefotiofur in poultry hatcheries in 2010.

**SWEDEN**

**Initiative:** Sweden banned AGPs in 1986\(^28\) with a system of agriculture extension and monitoring of antibiotic use in place but no resistance monitoring. Veterinarians were to prescribe antibiotics to solely prevent or cure disease and they were not permitted to profit from dispensing medicines.\(^29\) Guidelines on feed, medication, management and hygiene were made to help in reduction of antibiotic use. Since 2000, Swedish Veterinary Antimicrobial Resistance Monitoring (SVARM) has been detecting trends in resistance.

**Impact:** The total use of antibacterial drugs to animals in Sweden decreased by approximately 55 percent by year 2000 and a relatively low prevalence of antimicrobial resistance was maintained after the ban in 1986. Between 1984-2009, the antibiotic sales for animals decreased from an average of 45 tonnes of active substance to 15 tonnes.\(^30\)

**UNITED STATES OF AMERICA**

**Limited Initiatives:** Even after recognising the problem of antibiotic resistance about four decades ago, the US is far behind from EU in addressing it. In 1977, the US Food and Drug Administration (USFDA) proposed banning tetracyclines and penicillins as additives in the livestock feed which is yet to be implemented.\(^31\) While public health advocates are contesting to prohibit these and other antibiotics in feed, the USFDA stating that the procedure is time consuming has decided otherwise. It believes that the industry is responsive in general and therefore has opted for a much criticised voluntary approach to address the issue of resistance.

In 2012-13, it came up with two policy documents known as Guidance for Industry to phase-out the use of medically important antimicrobials in food animals for production purposes and to bring the therapeutic uses of such drugs under the oversight of licensed veterinarians.\(^32,33\) It asked the drug companies to remove ‘growth promotion’ from their product labels and intends to control it through provisions of extra label use. This is much different from EU member countries which have successfully put mandatory bans on antibiotic growth promoters. Also, in the name of judicious use, the guidance has allowed antibiotic use for mass disease prevention. While extra-label use is prohibited for certain antibiotics over the last several years, it is largely considered a less effective approach. Such antibiotics include chloramphenicol, fluoroquinolones and cephalosporins.\(^34,35\)

**Limited impact:** While the initiatives are considered as a first step, they are largely being viewed as much delayed and less than required to help the growing problem of resistance in the US. Neither there is any reduction in the amount of antibiotics used in food-producing animals over the years. About 80 percent of antibiotics produced in the US is used for non-human use (see Table 3).

Across the retail chicken meat and in chicken, high level of resistance is found against several medically important antibiotics in bacteria of importance such as *Salmonella*, *Escherichia coli*, *Campylobacter* and *Enterococcus*.\(^36\)

| Table 3: Antimicrobials sold and distributed for food-producing animals and humans, USA |
|-----------------------------------|------------------|
| Amount of antibiotics sold for use in food-producing animals, 2011 | 13542 tonnes |
| Amount of antibiotics sold for human use in 2011 | 3289 tonnes |
| Increase in total antibiotics sold for use in food-producing animals, 2009-2011 | 475 tonnes |
| Percentage increase in amount sold for use in food-producing animals, 2009-2011: lincosamides, penicillins and tetracyclines | 64%, 44%, 22% |

Source: Centre for Science in the Public Interest: Antibiotic Resistance in Foodborne Pathogens
In retail chicken meat, between 2002 and 2011, the resistance was found to be increased in *Salmonella* and certain *Campylobacter* (*C. jejuni*). Against third-generation cephalosporins about 35.5 percent *Salmonella* were resistant compared to 10 per cent. Against ampicillin this reached to 40.5 percent from 16.7 per cent. So was the case with *C. jejuni*, wherein against ciprofloxacin, the resistance increased from 15.2 per cent to 22.4 per cent. In 2011, about 45 percent of *Salmonella* was resistant to more than three antibiotic classes. Resistance in *Escherichia coli* against ceftriaxone, a third generation cephalosporin was higher than any other retail meat tested. From 2010, tetracycline resistance was also increased in both *C. coli* and *C. jejuni*.

The trends were similar in chickens. During 1997-2011, *Salmonella* resistance against tetracycline increased from 20.6 percent to 40.9 percent (see Fig. 2). *Salmonella* resistance also increased against ceftriaxone from 0.5 percent to 6.3 percent during this time. Resistance was found increased in certain *Campylobacter* spp. against ciprofloxacin and tetracyclines. *Enterococcus* resistance against tetracyclines has also increased. In 2011, about 63.5 percent of *E. coli* and about 39.3 percent of *Salmonella* were resistant to more than two antibiotic classes.

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**FIG. 2: Resistance in chicken against tetracycline**

![Graph showing resistance in chicken against tetracycline from 1997 to 2011.](https://example.com/figure2)

Source: National antimicrobial resistance monitoring system (NARMS), USDA

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**Surveillance programmes of countries**

Most of the AMR surveillance programmes include health animals, diseased animals, food and diseased humans. DANMAP also monitors resistance in healthy humans. Most test for resistance in *Salmonella*, *Campylobacter*, *Escherichia coli*, *Enterococci* and animal pathogens.
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