3

INTRODUCTION TO DANMAP

3. Introduction to DANMAP

3.1 The DANMAP surveillance system

DANMAP is a surveillance system with five key objectives:

- To establish the state-of-nation in regards to the use of antimicrobial agents in food animals and humans
- To carry out surveillance for the occurrence of antimicrobial resistance in bacteria isolated from food animals, food of animal origin (e.g. meat) and humans
- To identify areas for further research e.g. transmission or regarding possible associations between antimicrobial consumption and antimicrobial resistance
- To deliver data to veterinarians, medical doctors and other health professionals for the development of antibiotic guidelines for treatment
- To act as a knowledge base for authorities, academia and politicians when performing risk assessment and management, thus supporting decision making in the prevention and control of resistant bacterial infections

The monitoring programme was initially developed in 1995 by researchers, based on frequent discussions and exchange of knowledge and results from research. Since then, DANMAP has evolved into a governmentally supported organisation. However, much of the design of the programme, including participation of the human laboratories and referral of strains is based on a voluntary principle.

DANMAP surveillance relies on four equally important components: well-established and well-functioning diagnostic systems, well-designed and representative surveys, reliable registers as well as mutual trust and openness between all collaborators.

A positive effect of the regular meetings and exchange between stakeholders is that these prove helpful in other aspects, for example, by contributing to a common knowledge pool regarding laboratory methods. This ensures and contributes to continuous improvements and harmonisation of the laboratory work. Meetings across sectors and between different stakeholders also contribute to a better mutual understanding, facilitating development and work towards mutual goals.

Surveillance is a complex undertaking and DANMAP encompasses many different surveillance components and covers resistance in different populations and contexts.

Three categories of bacteria are always included in DANMAP:

- Human clinical isolates to reflect the antimicrobial resistance levels in the human population that seeks medical care
- Foodborne zoonotic bacteria along the whole farm-to-patient chain to monitor the levels of antimicrobial resistance in shared pathogens
- Indicator bacteria from healthy food-producing animals to monitor status of antimicrobial resistance in the animal reservoirs.

The National Food Institute (situated at Technical University of Denmark, DTU) and Statens Serum Institut (SSI) are responsible for data interpretation and output communication mainly via the annual DANMAP report. Interpretations are independent of policy, risk management and private industries.

The DANMAP programme is funded jointly by the Ministry of Health and the Ministry of Environment and Food. Support from the ministries has also helped build the databases and ensuring the registers, which the current surveillance system relies upon.

For further information on the development and history of DANMAP, please read chapter 2, "DANMAP – A 20 year perspective" in DANMAP 2015.

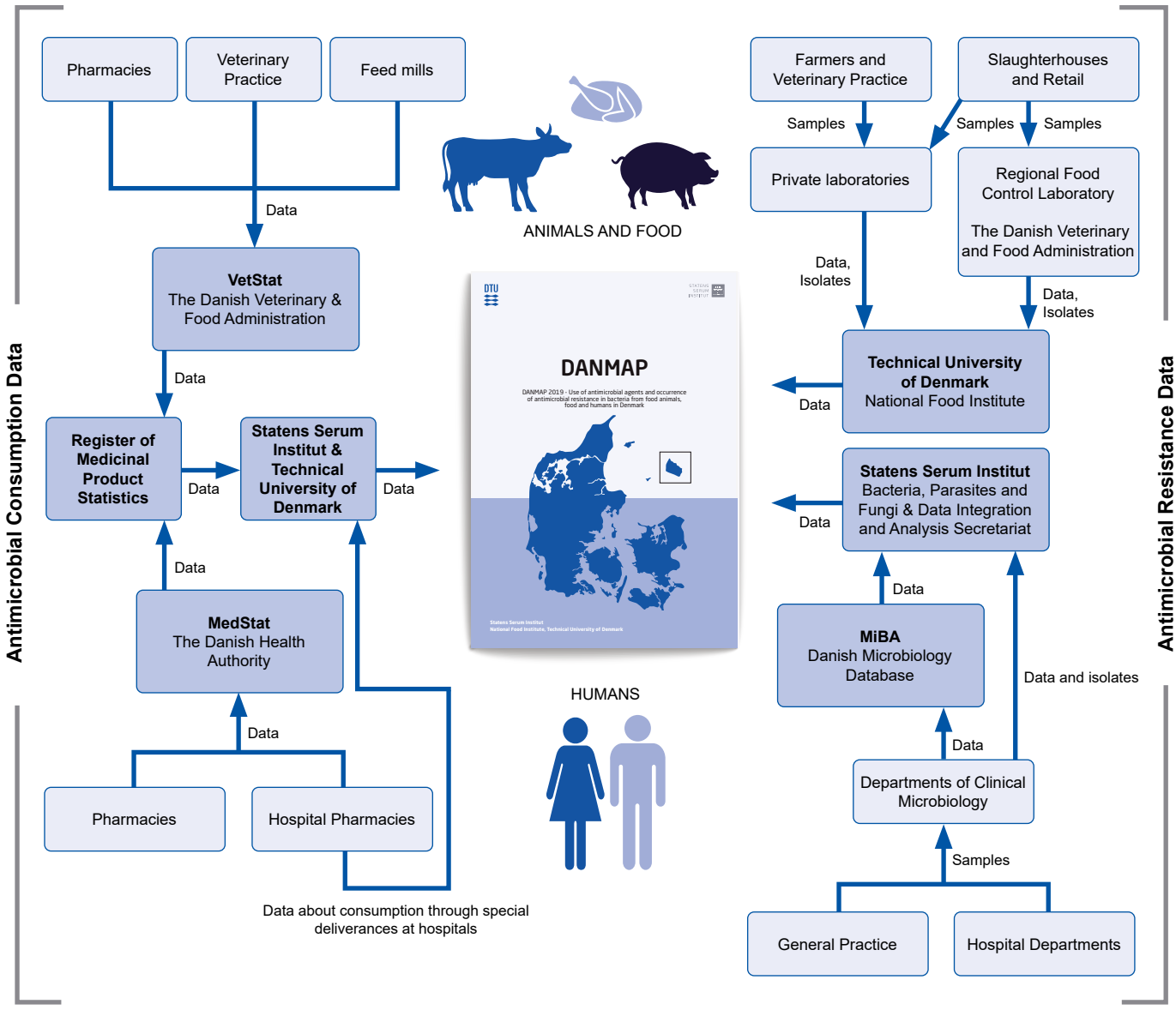
Organisation and data flow

Since 1995, a main purpose of DANMAP has been to monitor the entire chain from farm to fork to patient. The organisation and collection of DANMAP data and the interdisciplinary collaboration between sectors and organisations is presented in Figure 3.1.

The recent introduction of whole genome sequencing (WGS) has been a big step forward for surveillance purposes and in outbreak situations and has become routine standard in most reference laboratories. Whereas, phenotypical testing is still considered relevant, more feasible, cheaper and sometimes faster, especially in a clinical setting. Phenotypical testing also continues being used in combination with WGS to describe and determine which resistance genes are relevant to look for when using molecular analysis. Furthermore, it complies with EU regulations in food and animal testing.

Bacterial isolates from food, food animals and humans are submitted to the Regional Food Control Laboratory or occasionally the Technical University of Denmark and Statens Serum

Figure 3.1 Organisation of the DANMAP collaboration regarding data and data flow DANMAP 2019



Institut, respectively, for further phenotypic and genotypic characterisation (Figure 3.1). In 2019, WGS was extensively performed on selections of single isolates. These isolates were analysed for clonal relationship, as well as antimicrobial resistance genotypes (including ESBL, AmpC and CPO), and the presence of mobile elements such as plasmids. When specific clones carrying the same antimicrobial resistance genes are found in common among both food and human isolates, genomic data analysis such as core genome multilocus sequence typing (cgMLST) and single nucleotide polymorphism (SNP) calling, are used to examine possible transmission between the reservoirs. The choice of the methods in surveying different bacteria and infections is described in more detail in the different chapters and sections of the report.

3.2 Information on demographics and food production

The following sections present some general information for 2019 about the human population in Denmark and the included food production sectors. It also provides an overview of the antimicrobial agents used for therapeutic purposes in humans, and systemic and intramammary administration in animals in 2019.

3.2.1 Populations and productions

Human population and healthcare system

During the past two decades, the human population in Denmark has increased from approximately 5.2 million inhabitants in 1995 to 5.8 million in 2019 [www.dst.dk]. Simultaneously, the average age has increased gradually. In 2019, the national average age was 41.7 years. The population and the respective regional distribution, in 2019, is presented in Figure 3.2, while regional differences and changes in age are presented in Figure 3.3.

In Denmark, microbiological analyses are carried out by ten departments of clinical microbiology (DCMs) altogether, situated at the main regional hospitals in Denmark, also represented in Figure 3.2. The analyses performed cover all samples from public hospitals and most samples from general practitioners (GPs). In addition, some GPs perform culturing of urinary samples from their patients. In the Capital Region of Denmark one private laboratory also performs additional analyses for the GPs.

Figure 3.2 The five Danish healthcare regions and their respective population distributions. In addition, the ten DCMs are marked by black dots. The grey dot indicates the reference laboratories situated at SSI DANMAP 2019

North Denmark Region

No. of inhabitants	589,755
No. of inhabitants/km^2	75
No. of inhabitants/GP	1,934

Central Denmark Region

No. of inhabitants	1,320,678
No. of inhabitants/km^2	102
No. of inhabitants/GP	1,554

Capital Region of Denmark

No. of inhabitants	1,835,562
No. of inhabitants/km^2	717
No. of inhabitants/GP	1,700

Region Zealand

No. of inhabitants	836,738
No. of inhabitants/km^2	116
No. of inhabitants/GP	1,831

Region of Southern Denmark

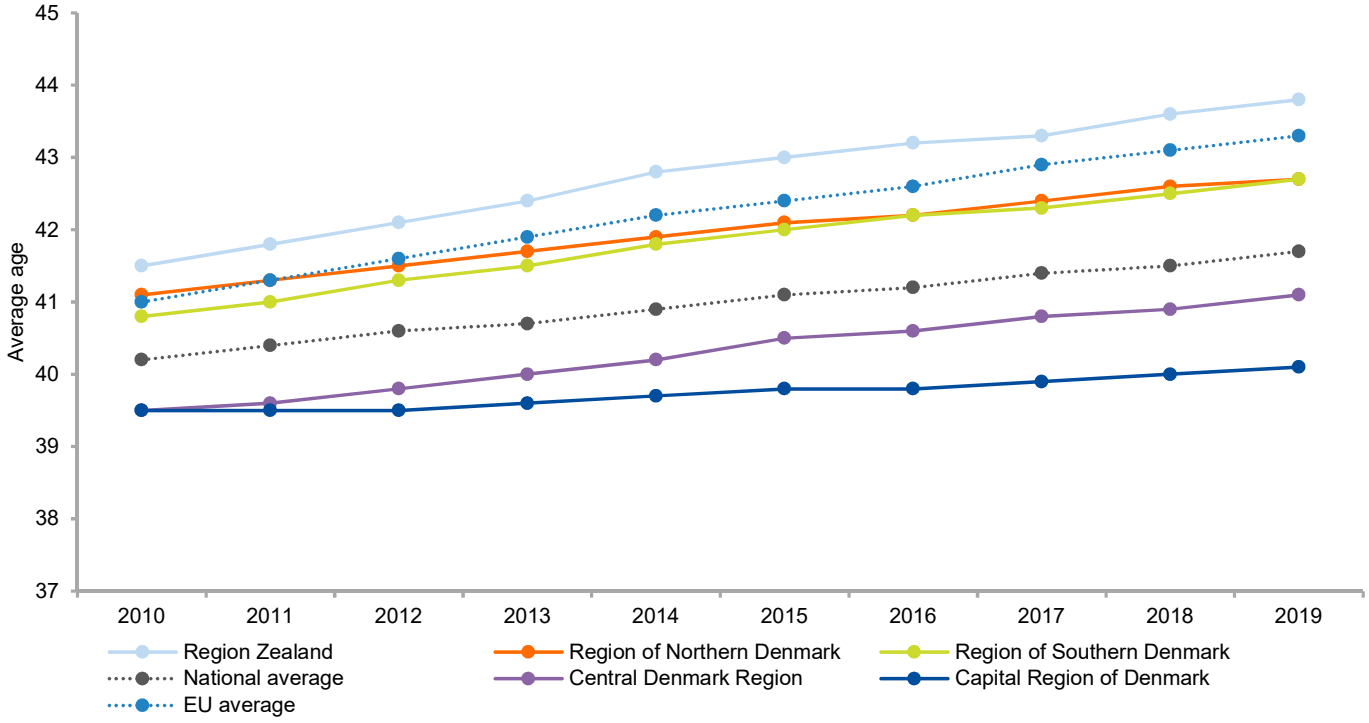
No. of inhabitants	1,223,348
No. of inhabitants/km^2	100
No. of inhabitants/GP	1,494

GP = general practitioner

DCM = department of clinical microbiology

Source: Statistics Denmark [www.dst.dk] and the Danish Medical Association [www.laeger.dk]

Figure 3.3 Changes in regional distribution of average age, Denmark DANMAP 2019



Animal population and food production system

Denmark is an agricultural country, with more than half of its area managed by the agricultural sector. The agricultural sector contributes to employment with around 146,000 jobs in the primary production and processing, and contributes around 24% of the Danish export earnings. Livestock is of great importance and approximately 25% of the agricultural enterprises are specialised in the production of livestock mainly pigs, cattle, chicken and mink [Danish Agriculture and Food Council, 2019].

The production of food animals and the production of meat and milk are presented in Table 3.1 and 3.2. In 2019, the number of pigs produced decreased by approximately 2% compared to 2018, and the number of exported fattening pigs (15-50 kg) continued to increase by approximately 3%.

Since 2004, the total exports of fattening pigs have increased more than seven-fold [Statistics Denmark, Danish Agriculture and Food Council, 2020].

The size of the Danish cattle production has changed slightly between years, and from 2018 to 2019, the number of dairy cows and cattle slaughtered decreased by 2-3%, while the amount of milk produced remained at the same level [Statistics Denmark 2020]. The number of broilers produced increased by 1% and approximately 16% of the broilers produced in Denmark in 2019 were exported for slaughter. The production of turkeys has fluctuated considerably over the past decade. Since 2006, more than 99% of the turkeys produced have been exported for slaughter, thus the majority of turkey meat available for sale in Denmark is listed as imported.

Table 3.1 Production (1000' heads) of food animals and mink, Denmark DANMAP 2019

Year	Pigs		Cattle		Poultry		Fur animals - mink	
	Total	Exported[a]	Slaughter cattle	Dairy cows	Broilers	Turkeys	Females	Kits
2010	28505	7074	519	574	117653	1184	2657	14638
2011	29399	7632	551	575	115454	960	2776	15325
2012	29047	8794	539	580	111080	1103	2936	16147
2013	28996	9318	551	574	117315	692	3143	17634
2014	29926	10517	556	563	115497	595	3296	17963
2015	30874	11563	513	561	114238	598	3387	18798
2016	31660	12771	540	571	120685	834	3161	17260
2017	31662	13679	509	570	117602	601	3410	18378
2018	32558	14028	533	575	122268	642	3385	17634
2019	31758	14542	518	567	123976	661	2495	13224

Source: Statistics Denmark [www.dst.dk] and The Kopenhagen Fur. Export data for poultry from Statistics Denmark (personal communication) and export of 15-50 kg live pigs from the Danish Agriculture and Food Council
a) Export of 15-50 kg live pigs. These are included in total number of heads, but antimicrobial use after export until slaughter is not registered as it takes place outside of Denmark

Table 3.2 Production (mill kg) of meat, milk and fish, Denmark DANMAP 2019

Year	Pork	Beef	Broiler meat[a]	Turkey meat	Milk	Farmed fish[b]	
						Land based	Marine net ponds
2010	1974	142	178	14	4830	42	11
2011	2008	145	175	9	4801	40	11
2012	1902	138	168	12	4928	44	14
2013	1896	140	177	8	5025	48	15
2014	1924	143	174	9	5113	47	14
2015	1954	135	172	9	5278	52	16
2016	1943	142	182	10	5376	49	12
2017	1896	135	178	7	5478	51	14
2018	1967	141	185	10	5615	53	14
2019	1870	137	187	8	5615	53	14

Source: Statistics Denmark [www.dst.dk]. Export data for poultry and average weight after slaughter from Statistics Denmark (personal communication)
a) In 2019, a final slaughtered weight of 1.62 kg per broiler produced and 12.0 kg per turkey produced were assumed
b) The numbers for 2019 are not final. Data now based on accounts statistics for aquaculture. The production of farmed fish includes fish transferred from one production facility to another

3.2.2 Registered antimicrobial agents

Table 3.3 shows the antimicrobial agents registered to treat bacterial infections in humans and animals respectively. Some of these are listed on the highest priority list of critically important antimicrobial agents for the treatment of bacterial infections in humans, according to definitions made by a working group under the World Health Organization [AGISAR, 6.revision, WHO 2019]. In order to be considered critically important, an antimicrobial must meet two criteria; 1) be the only - or one of a limited number of compounds available to treat serious human disease and 2) be used to treat infections caused by bacteria that are either possibly transmitted from non-human sources, or carry resistance genes from non-human sources.

In the newest revision from 2019, five drug classes were considered critically important and of highest priority: fluoroquinolones, 3rd, 4th and 5th generation cephalosporins, macrolides, glycopeptides and polymyxins. In addition, in Europe carbapenems are not allowed to be used in food production. In Denmark, the use of these drug classes in food animals has in general been low or been reduced through either voluntary or legislative restrictions, apart from macrolides, see chapter 4 for more information.

Furthermore, other antimicrobials may also be restricted due to national risk mitigation. For trends and preferred therapeutic choices in the antimicrobial treatment of humans and information on the national action plan from 2017, see chapter 5.

Growth promoters are no longer used for animals in Denmark and are shown in parentheses in Table 3.3. Most of these influenced Gram-positive bacteria. Since 1995, the indicator enterococci from animals and meat have been used as a measure of resistance towards former growth promoters.

Table 3.3 Antimicrobial agents registered for systemic and veterinary intramammary therapeutic use in animals and humans, Denmark DANMAP 2019

ATC / ATCvet codes[a]	Therapeutic group	Antimicrobial agents within the therapeutic groups	
		Animals	Humans
J01AA / QJ01AA, QJ51AA	Tetracyclines	Chlortetracycline, doxycycline, oxytetracycline	Doxycycline, lymecycline, tetracycline, tigecycline
QJ01BA	Amphenicols	Florfenicol	
J01CA / QJ01CA	Penicillins with extended spectrum	Ampicillin, amoxicillin	Ampicillin, pivampicillin, amoxicillin, pivmecillinam, mecillinam
J01CE / QJ01CE	Beta-lactamase sensitive penicillins	Benzylpenicillin, phenoxymethylpenicillin, procaine penicillin, penethamate hydroiodide	Benzylpenicillin, phenoxymethylpenicillin
J01CF / QJ51CF	Beta-lactamase resistant penicillins	Cloxacillin, nafcillin	Dicloxacillin, flucloxacillin
J01CR / QJ01CR	Comb. of penicillins and beta-lactamase inhibitors	Amoxicillin/clavulanate	Amoxicillin/clavulanic acid, piperacillin/tazobactam
J01DB / QJ01DB, QJ51DB	1st generation cephalosporins	Cefalexin, cefadroxil, cefapirin	Cefalexin, cefazolin
J01DC	2nd generation cephalosporins		Cefuroxime
J01DD / QJ01DD, QJ51DD	3rd generation cephalosporins incl. comb. with beta-lactamase inhibitors	Cefoperazone, ceftiofur, cefovecin	Cefotaxime, ceftazidime, ceftriaxone, ceftazidime/avibactam
J01DE / QJ51DE	4th generation cephalosporins	Cefquinome	Cefepime
J01DF	Monobactams		Aztreonam
J01DH	Carbapenems		Meropenem, ertapenem
J01DI	5th generation cephalosporins incl. comb. with beta-lactamase inhibitors		Ceftaroline fasamil, ceftolozan/tazobactam, ceftobiprol
J01EA	Trimethoprim and derivatives		Trimethoprim
J01EB / QJ01EQ	Short-acting sulfonamides	Sulfadimidine	Sulfamethizole
J01EE / QJ01EW	Combinations of sulfonamides and trimethoprim, incl. derivatives	Sulfadiazine/trimethoprim, sulfadoxine/trimethoprim, sulfamethoxasol/trimethoprim	Sulfamethoxazole/trimethoprim
J01FA / QJ01FA	Macrolides	Spiramycin, tylosin, tilmicosin, tylvalosintartrat, tulathromycin, gamithromycin, tildiprocin	Erythromycine, roxithromycine, clarithromycine, azithromycine, telithromycine
J01FF / QJ01FF	Lincosamides	Clindamycin, lincomycin	Clindamycin
QJ01XX[b]	Streptogramins	(Virginiamycin)	
J01GB / QJ01RA, QA07AA	Aminoglycosides	Streptomycin, dihydrostreptomycin, gentamicin, neomycin, apramycin, paromomycin	Tobramycin, gentamicin
J01MA / QJ01MA	Fluoroquinolones	Enrofloxacin, marbofloxacin, difloxacin, ibafloxacin, pradofloxacin	Ciprofloxacin, levofloxacin, moxifloxacin
QJ01MB	Other quinolones	Oxolinic acid	
QJ01MQ[b]	Quinoxalines	(Carbadox, olaquindox)	
J01XA, A07AA / Not in ATCvet[b,c]	Glycopeptides	(Avoparcin)	Vancomycin, teicoplanin, dalbavancin, oritavancin
J01XB / QA07AA[b]	Polypeptides (incl. polymyxins)	Colistin, bacitracin	Colistin
J01XC	Steroid antibacterials		Fusidic acid
J01XD,P01AB[c]	Imidazole derivatives		Metronidazole
J01XE	Nitrofurane derivatives		Nitrofurantoin
J01XX / QJ01FF	Other antibacterials	Spectinomycin	Methenamine, linezolid, daptomycin, tedizolide, fosfomycin
QJ01XQ	Pleuromutilins	Tiamulin, valnemulin	
QP51AG04	Antiprotozoals, sulfonamides	Sulfaclozine	
Not in ATCvet[b]	Oligosaccharides	(Avilamycin)	
Not in ATCvet[b]	Flavofosfolipols	(Flavomycin)	

a) ATCvet codes start with a Q
b) Animal growth promoters used before 1999 are listed in parentheses
c) Intestinal antiinfectives (A07AA) and imidazole derivatives for protozoal diseases (P01AB) were, for the first time, included in DANMAP 2014, since their widespread use in the treatment of *Clostridium difficile* infections makes them belong to the most used antibiotics in human infections in Denmark