Monitoring Antibiotic Consumption, Antibiotic Resistance, and the Presence of Antibiotic Residues in Luxembourg

Antibiotic resistance is bacteria's ability to withstand the effects of one or more types of antibiotics. It poses a significant threat to public health both in Europe and globally[1], leading to longer hospital stays, increased mortality rates, and therapeutic challenges. As part of the first National Antibiotics Plan 2018-2022 which was extended until 2024, combatting antibiotic resistance supports the global "One Health" approach. This strategy requires close collaboration across human, veterinary, and environmental sectors, as well as between countries, recognising the borderless nature of antibiotic resistance. To fulfil this objective, Luxembourg has produced its initial report on monitoring antibiotic consumption, resistance, and the presence of residues, compiling key national findings for the latest reporting year. This fact sheet summarises the report's salient outcomes, with the complete version accessible on the health portal website of the Grand Duchy of Luxembourg.

www.sante.lu/pna

Antibiotic Consumption in Human Health

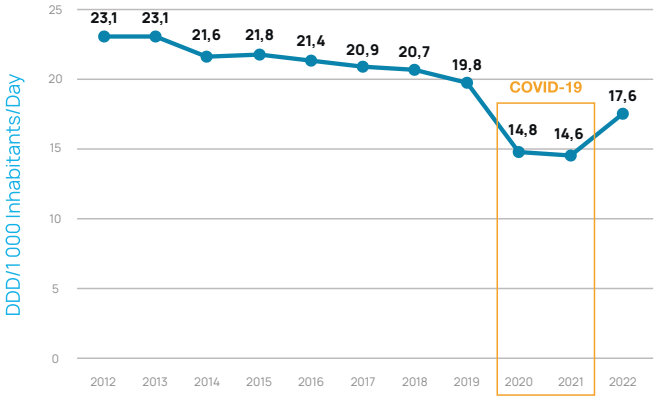
In 2022, antibiotic consumption in Luxembourg's community sector (community pharmacies) stood at 17.6 DDD[2]/1000 inhabitants/day, reaching a 20.5% increase compared to 2021, and just lower than the European average of 17.8 DDD/1000 inhabitants/day. Consumption of antibiotics has steadily declined since 2012. The significant drop in consumption in 2020 and 2021 can likely be attributed to COVID-19 containment measures (lockdowns, mask mandates, enhanced hand hygiene practices and widespread use of hand sanitiser). Consequently, there was a reduction in infections and likely also a decrease in inappropriate antibiotic prescriptions for mild, self-limiting infections due to restricted access to primary care during lockdowns. However, there was a rebound in consumption in 2022 following the relaxation of COVID-19 restrictions. Penicillins were the most frequently consumed antibiotics, followed by macrolides and cephalosporins.

In hospitals, antibiotic consumption reached 1.41 DDD/1000 inhabitants/day in 2022 when accounting for all hospital dispensations, reflecting a 10.2% increase compared to 2021. This figure falls below the European average of 1.60 DDD/1000 inhabitants/day and had been on a downward trajectory from 2012 to 2019. The apparent decline in 2020 and 2021 likely stems from the decrease in hospitalisation days during this period, resulting in fewer prescriptions. However, consumption rebounded in 2022. It's worth noting that data collection was standardised across hospitals in 2022, encompassing all types of dispensations, warranting caution in interpreting these findings. Penicillins emerged as the most widely consumed antibiotics, followed by cephalosporins and macrolides.

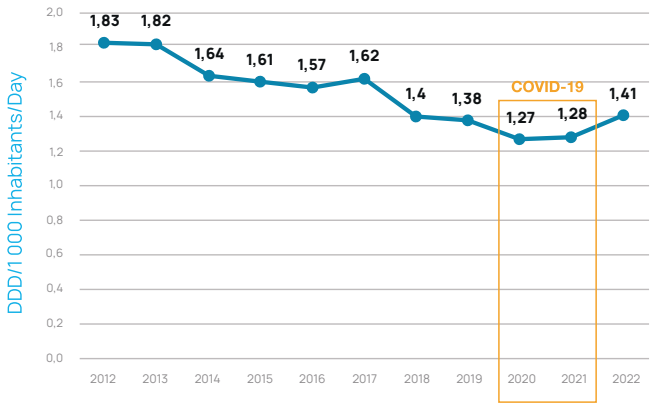
1 Antimicrobial Resistance (openwho.org)

2 DDD: Defined Daily Dose: a measure used to account for the use of medications, assumed to be equal to the average maintenance dose per day for a drug used in adults for its primary indication. Defined Daily Dose (DDD) (who.int)

Community Consumption



Hospital Sector Consumption

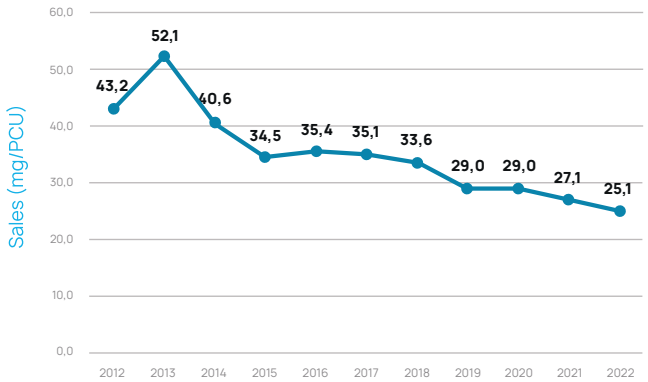


When focusing solely on antibiotics dispensed during full hospitalisations (stays of at least one night in the hospital), the consumption rate stood at 467.9 DDD/1000 hospital days in 2022. This means that a patient hospitalised for 10 days was treated with antibiotics for an average of 4.7 days. This consumption metric had not been calculated before 2022.

Antibiotic Consumption in Animal Health

In 2022, sales of antibiotics for animal health (livestock and companion animals), sourced from wholesalers in Luxembourg, reached 1.4 tonnes of active substance. The majority of these sales, amounting to 1.3 tonnes or 25.1 mg/PCU[3], targeted livestock. Among European nations disclosing sales data, Luxembourg ranks as the 6th smallest consumer (measured in mg/PCU). The top three classes of antibiotics sold in 2022 were penicillins, tetracyclines, and sulphonamides. These statistics relate to antibiotic sales within Luxembourg but do not accurately reflect the quantities dispensed. This is because antibiotics procured from abroad and dispensed in Luxembourg by cross-border veterinarians are excluded from the data. Hence, forthcoming data on veterinary antibiotic usage, collected since 2023, assumes significant importance as it promises a more precise depiction of actual antibiotic consumption in Luxembourg.

Sales of antibiotics for livestock decreased by 7.4% from 2021 to 2022 and have been steadily declining since 2013

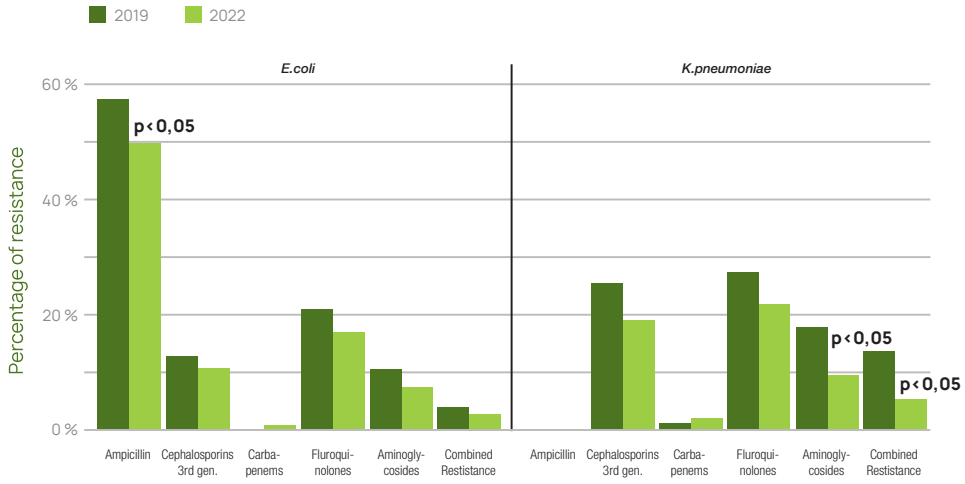


3 Population Correction Unit (PCU) : a theoretical measurement unit developed by the EMA. It considers the animal population of a country over a year (based on national statistics) and the estimated standard weight for each specific species at the time of antibiotic treatment. Conférence PNA 2023 (public.lu)

Antibiotic Resistance in Human Health

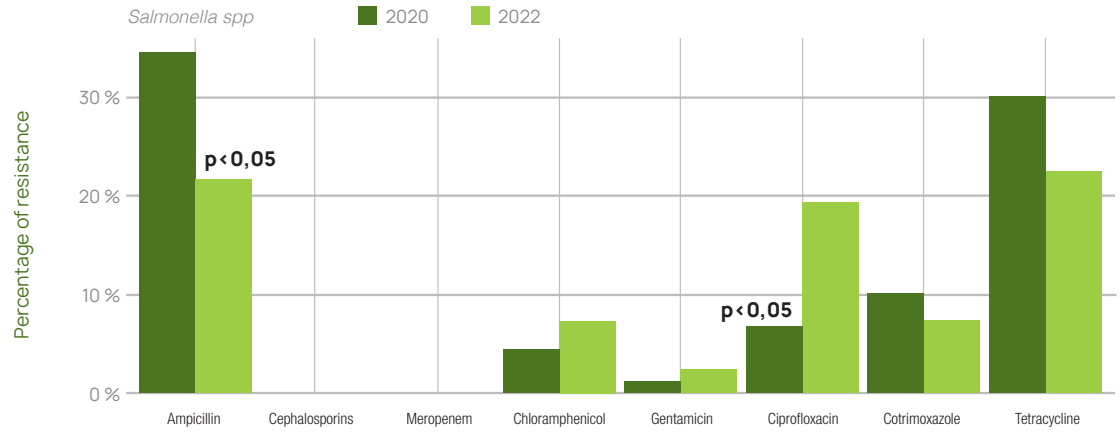
Antibiotic resistance is tracked through invasive samples collected in hospital settings, targeting the following pathogens: *Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Acinetobacter species, Streptococcus pneumoniae, Staphylococcus aureus, Enterococcus faecalis,* and *Enterococcus faecium.* In 2022, antibiotic resistance ranked below the European average for most microorganism and antimicrobial group combinations.

Ampicillin resistance in *Escherichia coli*, aminoglycoside resistance in *Klebsiella pneumoniae*, and combined resistance in Klebsiella pneumoniae have all significantly decreased from 2019 to 2022



Resistance is also monitored in cases of salmonellosis and Campylobacter infections as part of the surveillance of foodborne and waterborne diseases and zoonoses.

In salmonellosis, there was a significant decrease in ampicillin resistance and a significant increase in fluoroquinolone resistance from 2020 to 2022



The judicious use of fluoroquinolones remains imperative. Regarding *Campylobacter* infections, resistance to fluoroquinolones declined from 2020 to 2022, although it was notably higher than the European average in 2020. A comparison with the European average for 2022 is currently unavailable as this data has not yet been published.

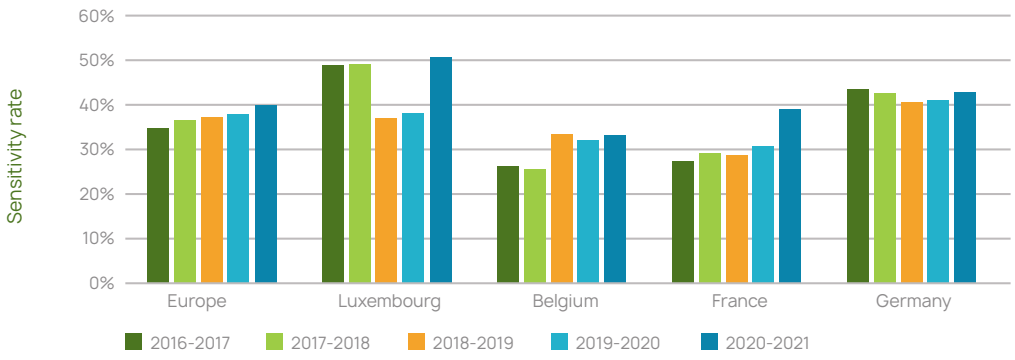
Antibiotic Resistance in Animal Health

As of now, surveillance of antibiotic resistance in animal health is exclusively centred on livestock. Resistance is monitored in bacteria including *Salmonella spp., Campylobacter coli, Campylobacter jejuni, indicator commensal Escherichia coli,* as well as ESBL* *Salmonella spp.,* AmpC** *Salmonella spp.,* CP*** *Salmonella spp.,* ESBL* *Escherichia coli,* AmpC** *Escherichia coli,* and CP*** *Escherichia coli.*

In 2021, 50.3% of *Campylobacter coli* exhibited resistance to two antibiotic groups, while 35.6% of isolates were resistant to a single group. Analysis spanning 2020 and 2021 revealed that 50.5% of indicator commensal *Escherichia coli* remained sensitive to all antibiotics tested.

During the examination of samples from sick livestock to pinpoint bacterial causative agents and determine optimal treatment strategies, administering aminopenicillins for calf diarrhoea posed a heightened risk of resistance. The most frequently isolated bacterial pathogen is *Escherichia coli,* with an 88.6% resistance rate to amoxicillin, decreasing to 24.1% when clavulanic acid is added.

In 2020-2021, the percentage of commensal indicator *Escherichia coli* bacteria sensitive to all tested antibiotics in Luxembourg is better than that of Europe and neighbouring countries



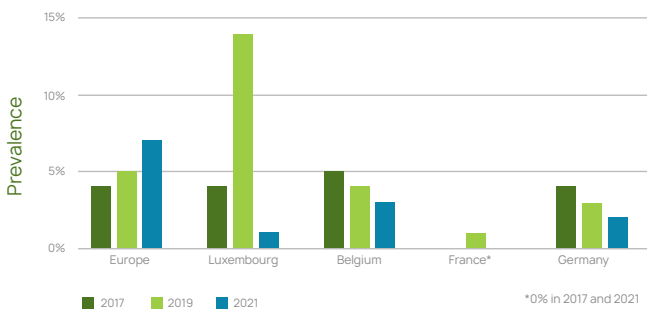
Food Safety

Meat products sourced from both retail markets and border control posts undergo sampling and analysis. The research zeroes in on bacteria such as *Salmonella spp., Escherichia coli ESBL**, AmpC**, or CP***, alongside indicator commensal *Escherichia coli*, and their respective resistances.

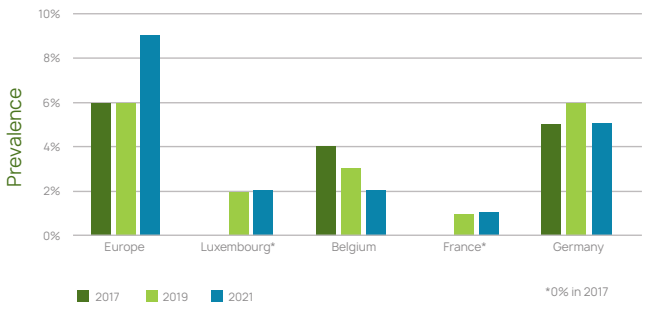
In 2020 and 2021, the prevalence of *Escherichia coli ESBL** and/or AmpC** in chicken, beef, and pork declined in Luxembourg but continued to exceed the European average in chicken meat.

Prevalence of E. coli ESBL and/or AmpC in meat (beef, pork and chicken) in Luxembourg, its border countries and in Europe (EU, Norway, Iceland and Switzerland) in 2017, 2019 and 2021

Beef



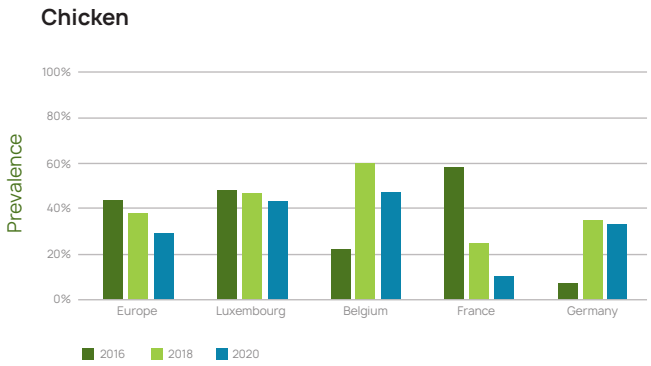
Pork



* ESBL: Extended Spectrum β-Lactamase

** AmpC: adenosine-monophosphate-cyclic β-Lactamase

*** CP: Carbapenemase-Producing



Presence of Antibiotic Residues in Our Environment

Studies on antibiotic residues in food items and animal feed revealed no traces in 2022.

Investigation into antibiotic residues in surface waters began with macrolides (clarithromycin, azithromycin, and erythromycin) before extending to other antibiotic categories. While some antibiotic residues were identified at low concentrations between 2016 and 2022, their health implications remain unassessed due to the lack of environmental quality standards, which are currently under discussion at the European level, coupled with the limited scope of analyses and residues examined.

The available data provides an insight into Luxembourg's current situation, allowing for ongoing monitoring of its trends year by year. It indicates that the country is positioned relatively well compared to its European counterparts. In future iterations, there will be a concerted effort to standardise the reference year across all areas, where feasible, enabling seamless tracking and correlation between different components. Moreover, there will be a keen focus on tracking Luxembourg's advancement in meeting the objectives outlined in the Council recommendation on stepping up European Union actions to combat antimicrobial resistance in a One Health approach[4]. Additionally, bespoke national goals aligned with the Council of the European Union's recommendation will be outlined.

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LNS LUXEMBOURG

Administration de la gestion de l'eau
Grand-Duché de Luxembourg

4 Council Recommendation on stepping up EU actions to combat antimicrobial resistance in a One Health approach (europa.eu)