Le système de surveillance français des salmonelles

Deuxième article

Structure du système français de surveillance des *Salmonella* de la ferme à l'assiette

Soumis à Zoonoses and Public Health

Salmonella est un pathogène zoonotique alimentaire qui fait, en France, l'objet d'une volonté de lutte intégrée de longue date, soutenue par le cadre réglementaire européen et s'appuyant sur un système de surveillance exemplaire, couvrant l'ensemble de la chaîne alimentaire, de la fourche à la fourchette. Le système de surveillance intégré des salmonelles en France repose à la fois sur des réseaux de surveillance passive (remontant à 1947 pour les cas humains et à la fin des années 80 pour les principaux réservoirs animaux) et sur un système de surveillance active qui a évolué de façon importante sur les 15 dernières années, sous l'influence de la réglementation européenne.

L'article suivant présente l'architecture du système de surveillance français, ses acteurs et les données produites. Pour chaque secteur, secteur humain puis secteurs vétérinaire et agroalimentaire, le contexte réglementaire européen est d'abord rappelé, puis l'organisation nationale de la surveillance est mise en lumière. La surveillance pour les secteurs vétérinaire et agro-alimentaire a été considérée en trois temps, surveillance des animaux de rente, surveillance des denrées alimentaires et surveillance de l'antibiorésistance. Chaque dispositif, qu'il soit actif ou passif, institutionnel ou non, a fait l'objet d'une analyse détaillée selon les critères de l'OIE (Office International des Epizootie) et de l'EFSA (European Food Safety Agency) concernant l'évaluation des systèmes de surveillance. Enfin, les forces et faiblesse du système, sa dynamique et sa capacité à répondre aux objectifs usuels de la surveillance sont discutées.

Le manuscrit présenté a fait l'objet d'une soumission à Zoonoses and Public Health et est en cours de révision.

Structure of the French farm to table surveillance system for *Salmonella*

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Summary

The French surveillance system is based on a pre-existing national system which can be traced back to 1947 for human cases and the late 80s for the main animal reservoirs. This system evolved under the combined levels of the European regulation and of changes in the observed prevalence of *Salmonella*. European regulation provides strong support to build an active harmonized surveillance system at farm level and for the integration of data throughout the food chain. The parallel existence of passive surveillance networks in the food and veterinary fields allows complementary information to be obtained on other sectors or points of measurement. The main weaknesses and strengths of this system are described and a comparison of the different approaches is presented through a grid analysis. Passive systems are very useful for detecting emerging or unusual events and for early warning of outbreaks. They also produce time series of cases or number of strains that can be used to assess the impact of interventions. Finally, active surveillance data, thanks to their representativeness and reliability, are key elements in the application of risk analysis tools such as quantitative risk assessment or attribution. Thus, despite the dispersal of the data between different actors, the collaboration of these actors at national level and their implication in European and international projects are effective and allow the main objectives of a surveillance system to be addressed.

Bullet points

This review describes the long lasting integrated surveillance system of *Salmonella* in France which evolved in the European regulatory framework and is one of the most performing ones.

It relies on an active surveillance system based on national and European regulations completed by a passive surveillance system composed of several networks.

This system, relying on several different actors, allows treating most of the missions of any surveillance system, from the investigation of outbreaks to complex approaches such as human cases attribution.

Introduction

In the context of the industrialization and the globalization of the food supply, of risk behaviours among consumers (raw eating, undercooking, poor kitchen hygiene) and of the steady increase of susceptible populations such as the elderly and immune-deficient patients, foodborne diseases remain a priority issue despite all the efforts made to prevent them (Sofos 2008).

Human salmonellosis reported in Europe has decreased over the past three years, but *Salmonella* remains one of the most frequently reported causes of foodborne zoonoses (Anonymous 2009). For the period 1995-1999, the French Institute for Public Health (InVS) estimated the total annual number of confirmed cases in France to be between 30,600 and 41,140, of which 92 to 535 led to the death of the patient (InVS 2004).

Moreover, antimicrobial resistance (AMR) has been described in *Salmonella* to antimicrobials used to treat acute gastroenteritis in human (third generation cephalosporins, fluoroquinolones) and has been defined as a risk factor increasing morbidity and mortality in humans (Molbak 2005). It is thus of the utmost importance to control the transmission of *Salmonella*, and consequently that of resistant strains of *Salmonella*, from animals to humans and to monitor antimicrobial resistance levels.

To determine optimal management measures to control this zoonosis, it is necessary to assess the risk of consumer exposure associated with the *Salmonella* contamination of food throughout the food chain. This requires information on prevalence, serotypes, antimicrobial resistance, food consumption, etc…. In this context, monitoring systems for *Salmonella* have been implemented in the human and the agro-food sectors. Such systems must include a trained field force, diagnostic laboratory support, data collection and analysis capabilities (Hueston 1993). To have a global overview of the surveillance systems involved in *Salmonella* monitoring in France and to analyse their specificity and complementarity, an analysis grid has been defined based on OIE (terrestrial animal health code, chapter 6.5) and the European Food Safety Authority (EFSA) guidelines (2006) and has been applied following the usual evaluation steps (CDC 2001). Only current surveillance systems have been included in this analysis.

This paper thus presents the structure, limits and evolution of the French surveillance system relating to *Salmonella* within the framework of the European “farm to table” monitoring approach, focusing on the main reservoirs: food animals and related products.

1 Architecture of the *Salmonella* surveillance system

Salmonella, as a zoonotic pathogen, is the subject of several European regulations. This chapter presents the European regulatory framework and the organization of the national surveillance system, from human cases to animal sources. The actors involved in this system have previously been described by Dufour and La Vieille (Dufour and La Vieille 2000) (Figure 1).

1.1 Human sector

1.1.1 European regulatory framework

The surveillance of sporadic salmonellosis (i.e. not associated with an outbreak) is not regulated at European level. However, surveillance of communicable diseases based on networking of expertise in the EU Member States is promoted by Commission Decision 2119/98/EC. In 2005, under the Zoonosis Directive (Directive 2003/99/EC), the investigation and reporting of foodborne outbreaks became mandatory (Gervelmeyer, Hempen et al. 2008). At the same time, the European Centre for Disease Prevention and Control (ECDC) was established (Regulation (EC) no. 851/2004) in order to enhance the capacity of the Community and the Member states to protect human health through the prevention and control of human diseases. As far as reporting is concerned, EFSA and ECDC jointly analyze all data from the human and agro-food sectors. The results are published in an annual Community Report (2009).

1.1.2 National surveillance system (table 1)

The declaration of foodborne outbreaks has been mandatory in France since 1952 (Decree no. 52-953 of 7 August 1952), allowing outbreak cases surveillance. Foodborne outbreaks are defined as a group of at least two cases with mostly digestive symptoms that can be linked to a common food source. An outbreak will be confirmed as caused by *Salmonella*, if a *Salmonella* strain is isolated from a sample coming either from one of the patients or from the suspected food item. Outbreaks must be notified to either the official “départemental” (“départements” are subdivisions of the national territory administered by a Prefect) sanitary or veterinary services (named DDASS or DDSV respectively). InVS centralizes those data at national level. The DDSV and DDASS databases are merged and

duplicate data are eliminated. In 2007, data on 1,436 foodborne outbreak cases associated with *Salmonella* were centralized. For some outbreaks, specific epidemiological investigations are performed, using data collected during further enquiries and data provided by the National Reference Centre (NRC) and the *Salmonella* Network for the food data (described below in § 1.2.2.2) (Espié, Weill et al. 2005a; Espié, De Valk et al. 2005b; Dominguez, Jourdan-Da Silva et al. 2008). Descriptive results and epidemiological studies are published in the weekly epidemiological bulletin (Bulletin épidémiologique hebdomadaire, http://www.invs.sante.fr/BEH/) and in scientific publications (Vaillant and Espie 2005; Brouard, Espié et al. 2007; Jourdan, Le Hello et al. 2008).

No mandatory notification is required for sporadic salmonellosis cases. However, passive laboratory-based surveillance of *Salmonella* detection from human samples, carried out by NRC since 1947, allows the collection of data on sporadic cases. This surveillance system relies on a stable network of voluntary clinical laboratories (private or hospital-based) representing 30 to 40% of all French clinical laboratories involved in human medicine. Laboratories send NRC either strains of *Salmonella* or reports on the strains isolated and serotyped on a daily basis. Strains and reports are registered together with epidemiological information such as travel, age and sex of the patient, type of sample taken (stool, blood…) or geographic location. A biological specimen bank and a national database on human strains are constituted. NRC registers data on about around 10,000 cases a year. Statistical analyses are performed on a weekly basis to detect unusual events, and all surveillance data are communicated to InVS. Data and analysis are published in the annual activity report of the NRC (http://www.pasteur.fr/sante/clre/cadrecnr/salmcnr/salmcnr-actualites.html) and through scientific publications(Weill, Guesnier et al. 2006).

1.2 Agro-food sector

1.2.1 European regulatory framework

Salmonella in food animals

The first step in *Salmonella* surveillance in food animals at European level was the implementation of Council Directive 1992/117/EC. This Directive concerned measures for protection against specified zoonoses and zoonotic agents, in animals and products of animal origin, in order to prevent outbreaks of foodborne infections. One goal of Directive 1992/117/EC concerned the control of *Salmonella* in the

Gallus gallus species, i.e. broilers and laying hens, focusing especially on the eradication of the serotypes Enteritidis and Typhimurium in breeding animals.

In 2003, this Directive was replaced by Directive 2003/99/EC of the Council and Parliament and Regulation (EC) no. 2160/2003. Directive 2003/99/EC on the monitoring of zoonoses and zoonotic agents aims to improve and coordinate the monitoring of zoonotic agents in the Community and to collect data that is easier to compile and compare. This should enable hazard identification and characterization, and exposure assessment related to zoonotic agents. *Salmonella* and its antimicrobial resistance are covered by this harmonized monitoring. Regulation (EC) no. 2160/2003 describes the progressive and proportionate organization of the control of *Salmonella* and other specified foodborne zoonotic agents at European level. Member States must implement programs to reduce the prevalence of *Salmonella* in farm animals and products of animal origin. Poultry (broilers, laying hens and turkeys) and pigs, considered as the major animal reservoirs, are the first productions concerned by these control measures at breeding and production level. Within this framework, harmonized prevalence studies, so-called “baseline studies”, have been conducted since 2004, to obtain scientifically relevant data about the initial level of prevalence in each Member State. On the basis of these results, mitigation targets are set species by species for specified serotypes. For example, a maximal prevalence of 1% must be met for the serotypes Hadar, Infantis, Virchow, Enteritidis and Typhimurium by the end of 2009 in breeding flocks of laying hens and broilers (Regulation (EC) no. 1003/2005).

***Salmonella* in food**

In 2002 the European Parliament adopted the “Food Law”, (Regulation (EC) no. 178/2002), laying down the general framework to ensure a coherent approach in the development of food legislation from farm to table; EFSA was created as part of this framework. The “Food Law” establishes principles and responsibilities, the means of providing a strong scientific base, efficient organizational arrangements and procedures to underpin decision-making in matters of food and feed safety. The principle of transparency for the consumer is also established. A package of three regulations and one directive constitutes the food hygiene legislation dedicated to food business operators (FBO) and is completed by two other regulations relating to official controls and feed hygiene.

General rules for FBOs, including primary production, are laid down by Regulation (EC) no. 852/2004. FBOs must ensure that their products satisfy the hygiene requirements set by Regulation (EC) no.

2073/2005 laying down the microbiological criteria and the implementation of hygienic rules. One of the criteria set is the absence of *Salmonella* in the product for safety criteria (i.e. defining the acceptability of the product) and at specific stages of the process for process hygiene criteria (i.e. setting an indicative contamination value above which corrective actions are required). This is to be met according to HACCP (Hazard Analysis Critical Control Points) principles and be scientifically justified. To ensure verification of compliance with the "Food Law", official controls are performed according to Regulation (EC) no. 882/2004. They must be planned on the basis of risk assessment, relying on a scientific approach, in order to obtain an objective selection of products and operators to be controlled.

Antimicrobial resistance in food animals

Since the end of the nineties, several international scientific reports and recommendations have led to publications recommending the harmonization of surveillance and the regulation of foodborne antimicrobial resistance and the use of antimicrobials in animals, based on public health concerns (WHO, 1997 and 1998; Copenhagen, 1998; FAO/WHO/OIE 2003 and 2007, Codex 2005, OIE 2006). Consequently, a European strategy against the microbial threat has been defined in agreement with the "precautionary principle". The use of antimicrobials as growth promoters in animal productions has been banned (Council Regulations (EC) no. 2821/98 and (EC) no. 2788/98). At the same time, surveillance systems for non-human use of antimicrobials and for antimicrobial resistance have been implemented at all levels of the food chain and a Community Reference Laboratory has been nominated and financed to promote harmonization of the methods used to assess antimicrobial resistance. For *Salmonella*, a harmonized continuous monitoring system in food animals is being implemented on the basis of a selection of strains isolated during the mandatory control programs (Decision 2007/407/EC**)**. National data on antimicrobial resistance have had to be declared to and have been published by EFSA since 2003 (2009).

1.2.2 National surveillance system

The national surveillance system for *Salmonella* in the agro-food sector relies on active institutional surveillance coordinated by the French Food Directorate (DGAL) operating under the European regulatory framework, completed by a passive system based on networks centralizing non-human

strains of *Salmonella* from public and private veterinary laboratories. Both active and passive surveillance systems are presented following.

Active surveillance system

Salmonella in food animals (table 2)

Based on a pre-existing voluntary program, the continuous mandatory monitoring and control plan in breeding flocks of *Gallus gallus* has been implemented in France since 1999 in accordance with Directive 1992/117/EC. The serotypes Enteritidis and Typhimurium were targeted in breeding flocks of broilers and laying hens until 2007. Since 2007, this plan has evolved in line with Regulation (EC) 2160/2003 and its implementing regulations concerning the control of *Salmonella*. It is in the process of being widened to include turkeys and pigs, all species being monitored at breeding and production level, and is still targeted on the serotypes Enteritidis and Typhimurium. In *Gallus gallus* breeding flocks, 3 more serotypes are regulated: Hadar, Infantis and Virchow. These regulated serotypes are defined as notifiable disease submitted to sanitary policy measures (Rural Code, article D223-21). However, information on all the serotypes will be made available thanks to the classification of all *Salmonella* serotypes as notifiable diseases not subject to sanitary policy measures (Rural Code, article D223-1) for the regulated animal sectors. The continuous monitoring program concerns all flocks and herds and is thus exhaustive for the regulated sectors. This should lead to an annual database giving information on the national prevalence of the different *Salmonella* serotypes and their evolution in the regulated animal species at farm level.

To prepare the enforcement of these monitoring and control programs, the initial level of prevalence of *Salmonella spp* has been evaluated through baseline studies between 2004 and 2009. Sampling plans have been designed to assess a prevalence of 20 to 50 % (according to the species) with a precision of 3 to 5%. They have been conducted under the responsibility of DGAL, by national and departmental veterinary services in collaboration with the National Reference Laboratory (NRL) for *Salmonella*.

Salmonella in food (table 3)

In accordance with the “Food Law”, DGAL implements national plans either to assess consumer exposure ("surveillance plans" providing science-based evidence) or to detect anomalies or non conformities by the FBO ("control plans"). In the first case, the sample is randomly defined; in the

second case, the sample is targeted on one type of food operator or one food category, including imported products. If necessary, the French food safety agency (AFSSA), as NRL, is consulted for the definition of the protocols. In accordance with Regulation (EC) no. 882/2004, control and surveillance plans performed by veterinary services are implemented on a yearly basis. The data collected give information on the prevalence of *Salmonella* in different food products, at the slaughterhouse and/or at retail level.

Antimicrobial resistance monitoring

Since 1999 the Food Directorate has supported monitoring plans for antimicrobial resistance in indicator and zoonotic bacteria in the major animal production sectors (pig, poultry and cattle). These plans have been managed by AFSSA in collaboration with the DDSV and public laboratories (LVD) since 1999 for broilers, 2000 for pigs and 2002 for cattle. These plans are still ongoing, but the search for *Salmonella* has been progressively abandoned (in 2004 for broilers and pigs and in 2008 for cattle) because of the low prevalence leading to an insufficient isolation of strains.

Since 2008, surveillance of antimicrobial resistance in *Salmonella* has been implemented in the regulated sectors (*Gallus gallus*, turkeys and pigs), beginning with laying hens in 2008. The strains tested for antimicrobial resistance come from the continuous monitoring and control plans with an upper limit of 170 per year and production. For the food sector, recent data have been collected under the national control and surveillance plans.

This surveillance activity has been included in the working plan of the NRL for antimicrobial resistance following technical recommendations of EFSA for European data harmonization. It should lead to information on antimicrobial resistance in *Salmonella* serotypes per animal species or food category.

Thus, the active institutional surveillance furnishes national data on the prevalence of *Salmonella* per serotype, with the flock or herd as epidemiological unit for food animals and the batch or carcass for food. Depending on the studies, the target populations include breeding animals, production animals or food categories, covering all the food-chain. The different studies are based on randomly chosen samples generally with stratification on the size of the farm or slaughterhouse, designed to be representative of national production for food animals and to target risk items for food. The continuous mandatory monitoring is exhaustive for the targeted productions. Long-term continuous mandatory

monitoring allows trends in prevalence and emergence of particular serotypes or resistance profiles to be analyzed, whereas transversal studies (baseline studies, control plans and surveillance plans) give isolated evaluations of the prevalence. The laboratories involved in this surveillance work under quality assurance and the NRL organizes inter-laboratory assays to ensure the harmonization of the methods. Data are analyzed either by the DGAL or the NRL for the baseline studies. The data collected in the context of harmonized European surveillance are further analyzed and published by EFSA in annual community reports. The data are all published on internal communication media and, for the food data, on the agriculture ministry website.

Passive surveillance system (table 4)

For several years, AFSSA has been managing several passive surveillance networks that provide data on *Salmonella* isolated in several sectors of the agro-food chain.

The epidemiological observatory in poultry farming network (RNOEA) was created in 1987 and is managed by the AFSSA laboratory at Ploufragan (Souillard, Toux et al. 2007). The objective is to give to veterinarians epidemiological information on diseases observed in poultry, to follow trends and detect emergence. This network alerts about major diseases in poultry. The available data for *Salmonella* will concern the distribution of serotypes among both pathogenic and healthy carriage strains found in poultry.

The French antimicrobial resistance surveillance in veterinary pathogens network (RESAPATH) was created in 1982. This network is managed by the coordinated action of two AFSSA laboratories, Lyon (for cattle and small ruminants) and Ploufragan (for poultry and pigs) (Jouy, Meunier et al. 2003; Botrel, Chazel et al. 2006). Its aim is to give scientific and technical advice to laboratories and veterinarians on antimicrobial resistance in pathogenic bacteria, including *Salmonella*, isolated from food-producing animals mostly exhibiting clinical signs. Data on trends and emergence of antimicrobial resistance in pathogenic *Salmonella* are produced by this network.

The "*Salmonella*" Network was created in 1997. This network is managed by the AFSSA laboratory at Maisons-Alfort and collects strains of non-human origin. Its objectives are to provide technical advice for *Salmonella* serotyping, give national temporal trends on *Salmonella* serotypes isolated throughout the food chain and detect emerging or unusual events (Moury, Fremy et al. 2006). Data available will

concern the distribution of serotypes and the antimicrobial resistance profiles among 13 to 14,000 non-human strains of *Salmonella* a year, covering the whole food chain (from animals to products).

All the networks' partners are private and public veterinary laboratories. In addition, veterinarians provide case records to the RNOEA. Microbial analyses are multicentric (partly performed by AFSSA for the *Salmonella* Network); only the results of biological tests or diagnostics are reported to the RNOEA or the Resapath. However, analyses are validated by inter-laboratory trials organized annually by AFSSA, for the *Salmonella* Network (serotyping) and the Resapath (antimicrobial resistance). In all cases epidemiological data are collected on the original sample (geographical data, date of sampling, product description). Duplication of data is not totally under control. For the *Salmonella* Network, antimicrobial resistance testing is performed on "independent" isolates defined as coming from the same parcel, belonging to the same serotype and sharing similar epidemiological data. For the RESAPATH, duplicate data are defined for strains isolated from the same animal or flock, the same date of sampling and sharing the same serotype and antibiotype. Descriptive data are regularly reported to the partners. Detection of unusual events is regularly performed on the number of isolates per serotype at the *Salmonella* Network.

Public networks available for professionals concerned and scientists have been described, but this description does not preclude the existence of other databases in France maintained by and available to private operators on specific topics. For example, specialized private networks focus on *Salmonella* isolation results on feedstuffs (Qualimat network) and on *Salmonella* strains isolated in the pork sector (http://www.ifip.asso.fr/actu/pdf/MA_aval.pdf).

2 Discussion/ conclusions

The surveillance of the agro-food sector in France relies on an integrated food-chain system implemented under the European regulations, completed by lab-based passive networks. European regulation offers strong support for surveillance in the agro-food sector, pushing forward the previously existing systems toward harmonized methodologies, systematic sampling at farm level in the main sectors (Zoonosis Directive), risk-based surveillance for food within the framework of the “Food Law” (Stark, Regula et al. 2006) and integration of antimicrobial resistance in the monitoring systems. The importance of harmonizing the surveillance tools (typing tools, analyses, …) is emphasized by many

authors (Batz, Doyle et al. 2005; Gerner-Smidt, Hise et al. 2006; Ammon and Tauxe 2007). It relies in Europe on the NRLs, coordinated by the Community Reference Laboratories through their technical support and the inter-laboratory assays they organize (Ellerbroek, Alter et al. 2009). The final objective of this *Salmonella* surveillance system is to contribute to the reduction of the incidence of human cases with the choice of a farm to table approach aimed at limiting contamination at each stage in the food chain. This is of the utmost importance as small improvements in animal health can lead to a significant reduction in human cases according to the model developed by Singer (Singer, Cox Jr. et al. 2007), and as no fail-proof way of assuring the safety of food items exists at any point in the food supply chain (Allard 2002).

Limits and threats

Many of the usual limits and structural threats encountered in health surveillance systems are not avoided in the French *Salmonella* surveillance tools.

The burden of salmonellosis is difficult to assess and is probably underestimated, as the reporting of human diseases in France is based both on mandatory notification of outbreaks and the centralization of passive laboratory results. These surveillance systems, as most foodborne and declarative surveillance systems, are subject to underreporting (Flint, Van Duynhoven et al. 2005) with the cases reported and registered being only a part of the effective burden (Angulo, Voetsch et al. 1998). The mandatory reporting of foodborne outbreaks related to *Salmonella* has been estimated by a capture-recapture method to represent 15% of all cases (Gallay, Vaillant et al. 2000). This may be linked to complex bureaucratic procedures (Herida 2008) and the unknown aetiology of most reported outbreaks (Gallay, Vaillant et al. 2000). Similarly, the extent of *Salmonella* animal carriage or food contamination is not precisely known. Mandatory exhaustive control plans and prevalence studies do not cover all species. Fowls, turkeys, pigs are surveyed at farm and slaughterhouse level, cattle and sheep are concerned by controls performed at slaughterhouse level, but other food animals can contribute to the transmission of *Salmonella* such as fish, ducks (Hald, Vose et al. 2004) or dairy animals and other products (Haeghebaert, Sulem et al. 2003; Lailler, Sanaa et al. 2005). No representative data are available for such sources. For sources concerned by prevalence studies or

an exhaustive mandatory control plan, it can also be noted that small herds are not included and that any investigator bias can not be excluded despite strong harmonization efforts.

Meanwhile, all sources are concerned by passive surveillance, but such systems suffer from a lack of representativeness and reporting delay. The willingness of the laboratories to participate in the networks can interfere, and selection bias can affect the human cases reported or the strains collected. In addition to biases due to the passive structure of networks, their multicentric design can lead to investigator bias. As an example, the epidemiological information associated with the strains is of unequal quality. As a result, the management of duplicates can be difficult. All these weaknesses are highly dependent on the functional quality of the network. The evaluation of such networks is therefore a necessary procedure to determine the reliability of the results (Hendrikx, Chazel et al. 2005).

In France, the actors involved in the integrated surveillance of *Salmonella* are numerous. It makes the centralization of the data difficult and leads to an unequal quality and heterogeneity in the data collected. For example, the epidemiological units and the subtyping tools applied are diverse. It can limit collaborative studies and data cross analysis. Moreover, this “multiple head” system has a non-negligible inertia in a context where there are an obligation to comply with European regulations and a constant evolution of prevalences and exposure. Thus, on the one hand, a few sectors, known for their potential high prevalences and major exposure are well monitored. But thanks to the control programs implemented, their prevalence levels are mitigated (the prevalences of Typhimurium and Enteritidis in *Gallus gallus* breeding flocks are already under 1% in France). On the other hand, other sectors (such as ducks, minor species…) which have a lower, but non-negligible consumption and may present high prevalence rates do not beneficiate of the active surveillance system.

Strength and opportunities

Some of the characteristics of this surveillance system, despite the inherent biases previously exposed, can also confer strengths on the system.

The multiple part surveillance system, made up of different independent networks and actors, allows a high level of specialization of each one with a clear definition of objectives, a strong involvement of participants and a good knowledge of the data and their characteristics. Each network has a strong

background. The fact that they are long established means that they are able to rely on stable and reliable networks. The networks of laboratories participating in passive surveillance systems such as those of NRC or AFSSA have remained stable over the years and cover all the territory. The resulting databases are therefore appropriate to detect trends or unusual events for both sporadic and outbreak-related cases and food source contamination.

Adaptation of the surveillance system to its subject evolution is also possible with such a flexible organization thanks to several independent tools. For example, the active antimicrobial resistance surveillance system was suspended for *Salmonella* in 2002 for poultry and pigs and more recently for cattle. Too few strains could be collected according to the prevalences reached, whereas on one hand an exhaustive control plan was implemented (in poultry production) and on the other hand a passive network (*Salmonella* Network) could collect more strains. Specialized passive networks can also evolve considering prevalence mitigation as for the RESSAB. The clinical salmonellosis in adult cattle network (RESSAB) created in 1996 was run by AFSSA until 2007. The objectives were to monitor the incidence of salmonellosis associated with digestive or abortive symptoms in adult cattle and to identify associated serotypes and antimicrobial resistance (Chazel, Buret et al. 2007). This network made information available on the prevalence of lab-confirmed clinical salmonellosis in cattle, but ceased its activity in 2007 when the incidence became too low.

In addition, independence of surveillance tools does not exclude close collaboration and harmonization such as between NRC and InVS, and with the *Salmonella* Network, reinforcing the complementarities of their databases (Kerouanton, Marault et al. 2007).

Complementarities are also obvious through the combination of active and passive tools. In a context of limited public resources allocation, active surveillance can not cover all sectors annually. This incompleteness of surveillance is partly addressed by the co-existing permanent passive system. In the same way, the national *Salmonella* surveillance system described here can also collect data belonging to non-food animal associated sources and cases. Official surveillance of the non-animal food sources, such as vegetables (Brandl 2006), is partly performed by the General Directorate for Competition Policy, Consumer Affairs and Fraud Control through annual surveillance and control plans. Non-food sources are also to be considered since an estimated 5% of the transmission of *Salmonella* is not food-mediated (Mead, Slutsker et al. 1999). Pets and especially exotic pets are known to be contamination sources (Woodward, Khakhria et al. 1997; Mermin, Hutwagner et al. 2004;

De Jong, Andersson et al. 2005; Finley, Reid-Smith et al. 2006) and human to human transmission has also been described (Todd, Greig et al. 2008). Those sources are not monitored actively, but as for non-animal food sources, some data are available through the *Salmonella* Network, which definitely offers a useful alternative to active surveillance for the sources, whatever they are. Finally, some private initiatives exist such as Qualimat (http://www.qualimat.org/), an association which runs an auto-control plan for *Salmonella* in raw materials with the participation of the feed manufacturers, and as the PFGE profiles database managed by the "Institut du Porc" (http://www.ifip.asso.fr/actu/pdf/MA_aval.pdf). This shows a global concern about *Salmonella* and a will to monitor and to control it covering all sectors, imperfectly, but efficiently. Because of these reasons, the multiplicity of the systems and actors can be revealed to be a positive point.

The success of integrated surveillance at a national level depends on the availability of high-quality, accessible and comparable data used for meaningful analysis and reporting. Such an effective surveillance system should improve the scientific basis, on the one hand, for the implementation of management measures and, on the other hand, for the evaluation of their impact and risk analysis.

Thus, the issues to be addressed by a surveillance system are diverse: detection of outbreaks, burden of illness and economic burden estimation, prevention, assessment of the impact of interventions, microbiological risk assessment (Desenclos, Vaillant et al. 2002). Close collaboration between the different actors in surveillance, public health and food safety authorities and the harmonization of methodologies between the human and agro-food sectors is a key point in addressing most of these issues (Batz, Doyle et al. 2005; Ammon and Tauxe 2007; Sofos 2008) and seems to be a success in France.

If passive networks often suffer from reporting delay and selection biases, their daily computerized databases are suited to an alert activity. The NRC performs weekly unusual event detection by time series analysis on its database. This allows the public health authorities concerned to be informed quickly and to trigger the investigation of the outbreaks detected. The epidemiological investigations coordinated by InVS rely on combined data across agro-food and human surveillance (namely the NRC and the *Salmonella* Network), which is made possible thanks to the harmonization of the laboratory methodologies. A similar approach is being implemented (Baroukh, Le Strat et al. 2008) by

the *Salmonella* Network which could allow earlier warnings, from the contamination of the food-chain onwards and thus possibly prevent outbreaks.

Sporadic cases require a different approach, based on prevention and risk-based interventions. Attributing the cases to the main food-animal reservoirs is of the utmost importance in conceiving and assessing the impact of such interventions ((ICMSF) 2006; Ammon and Tauxe 2007; Sofos 2008). Several approaches can be used to perform attribution. In the case of sporadic case attribution, it is necessary to dispose of representative data in the agro-food sector. Currently, a microbial subtyping attribution project is in progress in France (David, Danan et al. 2008). This approach could be implemented thanks to the active collaboration of all the different surveillance actors.

Based on the information provided by the different surveillance systems, management actions are implemented and should be evaluated regularly according to outcome indicators. In France, interventions have been enforced at farm level. The first line impact is the level of prevalence in flocks, but the real objective is the number of cases induced. Within the framework of European regulation, continuous control programs are implemented with prevalence mitigation targets defined according to the animal production concerned. In France, the impact of one-year prophylaxis in *Gallus gallus* demonstrated a reduction of the prevalence of *Salmonella* in breeding flocks from 3% in 2006 to 0.6% in 2007 for the five regulated serotypes. These results show the efficiency of the programs and the good level of sanitary conditions of breeding production in *Gallus gallus*. Furthermore, the impact of the national control program implemented in the breeding flocks of *Gallus gallus* from 1998 onwards on human cases has been evaluated through time series analysis by Poirier et al (Poirier, Watier et al. 2008), using NRC data. A 33% decrease was observed in the prevalence in the flocks, and a significant decrease in human cases was demonstrated between 1998 and 2003, up to 21% for cases associated with the serotype Enteritidis.

Finally, collaboration also operates on an international level. The French human public health and food safety authorities cooperate at European level with ECDC and EFSA, and the NRC is WHO collaborating centre for reference and research on *Salmonella*.

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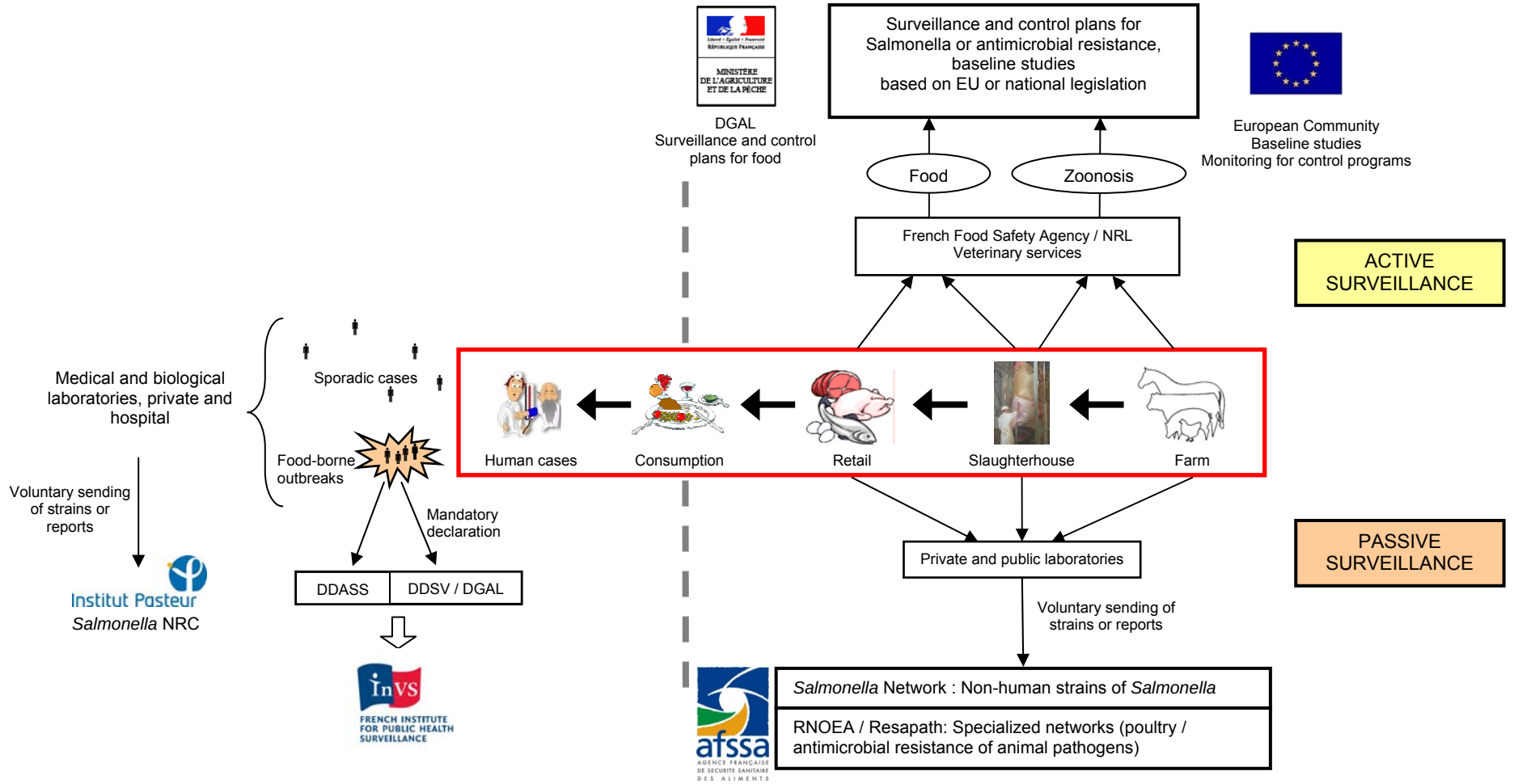

Figure 1: Organization of the *Salmonella* surveillance system in France in 2009

	National public health network: foodborne outbreak	National Reference Centre for Salmonella
Coordinator	InVS	NRC
Objectives	Registration of foodborne outbreak events with the biological agent, the food item involved and the number of cases	Temporal trends in serotypes and AMR of human cases Alerts in case of unusual events (number of cases)
Means of collection	Passive surveillance	Passive surveillance
Scope of surveillance	National	National
Monitoring period	Continuous since 1987	Continuous since 1947
Pivotal variable[a]	Number of outbreaks, number of cases per outbreak	Number of cases per serotype
Disease focus	General - multi-pathogens	*Salmonella* specific
Design	Descriptive + risk factors	Descriptive
Temporality	Trends	Trends
Availability of non pivotal information	Yes	Yes
Way of selection	Non-random	Non-random
Source of data	Mandatory disease notification	Laboratory investigation records and biological specimen banks based on an opportunistic collection
Coverage of the population	OK (mandatory).	2006: 1357 laboratories, among which 1028 private laboratories and 329 hospital laboratories, 30 to 40% of French clinical laboratories
Duplicates	Eliminated	Eliminated
Target population	Foodborne outbreaks occurring in France	*Salmonella* infected people
Study population	Foodborne outbreaks occurring in France that are notified	Cases confirmed by a laboratory collaborating with the NRC
Epidemiological unit	Outbreak	Strain
Case definition	Illness in at least two persons with digestive symptoms that can be attributed to the same food source	*Salmonella* strain identified in the sample
Laboratory testing	Not mandatory. For *Salmonella* confirmed outbreaks: private or hospital laboratory for identification of human cases of salmonellosis, NRC for serotyping. For veterinary isolates: LVD for identification and AFSSA for serotyping	Identification / Serotyping / Resistance phenotype (Disk Diffusion method, E-test) / Genotype (PCR, PFGE, MLVA, BLSE)
Data collection and management	DDASS, DDSV, InVS	NRC
Analytical methodologies	Descriptive. Case-control studies or cohort studies can be conducted using data that do not exist in the mandatory notification of foodborne outbreak	Descriptive Specific for unusual event detection
Quality assurance	For missing or invalid data, further enquiries at the DDSV or the DDASS	Enternet quality control "Quality approach" of the Pasteur Institute
Bias	Importance of the clinical symptoms Availability of samples to identify the biological agent Diffuse outbreaks Family outbreaks are less reported than collective or commercial catering outbreaks	Importance of the clinical symptoms Willingness of the laboratories to participate Population groups at risk
Reporting	Report: Weekly epidemiological bulletin, scientific publications	Annual report, scientific publications

Table 1: Surveillance of human cases in 2008

a: variable describing the quantity corresponding to the main objective of the survey.

	European control programs	European baseline studies
Coordinator	DGAL	DGAL
Objectives	Control of *Salmonella* prevalence in poultry	Evaluation of the prevalence level of *Salmonella* at farm level or at the slaughterhouse level
Means of collection	Active surveillance	Active surveillance
Scope of surveillance	National	National
Monitoring period	Continuous since 2007 (1998 for Enteritidis (SE) and Typhimurium (ST) in breeding flocks)	12 months, from 2004 to 2009 according to the channel
Pivotal variable	Prevalence: SE, ST, Hadar, infantis, Virchow for breeding flocks (laying hens and broilers) and SE, ST for production flocks of laying hens and broilers	Prevalence per serotype
Disease focus	*Salmonella* specific	*Salmonella* specific
Design	Descriptive + risk factors	Descriptive + risk factors
Temporality	Trends	Single occurrence
Availability of non pivotal information	Yes	Yes
Way of selection	Structured	Structured
Methods of selection	Exhaustive	Random selection Stratification on the farm or slaughterhouse size
Representativeness	Not relevant	OK
Target population	Breeding flocks (from 2007 on), laying hens (from 2008 on), broilers (from 2009 on)	Production and breeding flocks of laying hens, broilers, pigs and turkeys Flocks or animals either at farm level and/or at the slaughterhouse
Study population	Registered farms Breeding flocks: over 250 animals Production flocks of laying hens: over 250 animals delivered to a conditioning unit Production flocks of broilers: all the flocks except under 250 directly delivering to the consumer	Laying hens, broilers, pigs and turkeys farms or slaughterhouses Farms registered with a minimal size Slaughterhouses with a minimal size
Epidemiological unit	Building	Flock or herd
Case definition	At least 1 positive sample for broilers, at least 2 consecutive positive samples for breeders and laying hens	At least 1 positive sample
Laboratory testing	Laboratories with accreditation isolation / identification / serotyping (NFU 47100)	NRL for *Salmonella* Isolation / identification / serotyping
Data collection and management	DGAL / Veternary Services Direction	DGAL / NRL
Analytical methodologies	Descriptive (investigation if contamination)	EFSA, Specific / NRL at national level
Quality assurance	Certified laboratories	NRL / certified laboratories
Validation (bias)	Small flocks not included Direct selling of broilers not included Multicentric (investigator bias)	Small flocks and slaughterhouses not included Detection (a few units per building or band at the slaughterhouse)
Reporting	Annual Community report Intern communication	EFSA reports / NRL scientific publications

Table 2: Surveillance of food-animals in 2008

	Surveillance plans	Control plans
Coordinator	DGAL	DGAL
Objectives	Evaluation of the prevalence level of *Salmonella* in carcasses and products Specific questions such as comparison of sampling methods	Evaluation of the prevalence level of *Salmonella* on carcasses and products
Means of collection	Active surveillance	Active surveillance
Scope of surveillance	National	National
Monitoring period	several months to one year	several months to one year for broiler meat
Pivotal variable	prevalence (spp or per serotype)	prevalence per serotype
Disease focus	*Salmonella* specific	*Salmonella* specific
Design	Descriptive	descriptive
Temporality	Single occurrence	single occurrence
Availability of non pivotal information	No	No
Way of selection	Structured	Structured
Methods of selection	Random selection of slaughterhouses stratified on the size Random selection of the units	Random selection of the slaughterhouses or producers or targeted selection according to specific activities
Representativeness	OK	OK
Target population	Carcasses from the targeted channels Products in approved firms	Carcasses from the targeted channels Meat products: poultry, minced and mechanically separated meat
Study population	Food animals slaughtered in the selected slaughterhouses, products or retail units available in the targeted firms (producers or retail)	Pigs, large cattle and sheep slaughtered in the selected slaughterhouses Products in the selected factories
Epidemiological unit	Carcass, retail unit	Carcass, batch
Case definition	At least 1 positive sample	At least 1 positive sample
Laboratory testing	Laboratories with accreditation or LDA and AFSSA isolation / identification / serotyping (ISO 6579)	LVD isolation / identification / serotyping
Data collection and management	DGAL	DGAL
Analytical methodologies	Descriptive and specific	Descriptive
Quality assurance	COFRAC accreditation for meat products ISO 6579	COFRAC accreditation for meat products ISO 6579
Validation (bias)	Large flocks at higher probability of being sampled Multicentric (investigator bias)	Large flocks at higher probability of being sampled Multicentric (investigator bias)
Reporting	Memos, internal communication Report (synthesis) on the agriculture ministry website	Memos, internal communication Report (synthesis) on the agriculture ministry website

Table 3: Surveillance of food in 2008

	Salmonella Network	Resapath	RNOEA
Coordinator	AFSSA	AFSSA	AFSSA
Objectives	Spatio-temporal trend analyses of *Salmonella* throughout the food chain and detection of unusual events	Spatio-temporal trend analyses and emergence detection of antimicrobial resistance in veterinary pathogenic bacteria	Spatio-temporal trend analyses and emergence detection of poultry diseases
Means of collection	Passive surveillance	Passive surveillance	Passive surveillance
Scope of surveillance	National	National	National
Monitoring period	Continuous, since 1997	Continuous, since 1982	Continuous, since 1987
Pivotal variable	Strain number per serotype	Strain number per animal channel and pathology	Notification number (contaminated flocks and/or disease diagnostic notifications)
Disease focus	*Salmonella* specific	Multi-pathogens	Multi-pathogens
Design	Descriptive	Descriptive (+ transversal studies)	Descriptive
Temporality	Trends	Trends	Trends
Availability of non pivotal information	Yes	Yes	Yes
Way of selection	Non-random	Non-random	Non-random
Source of data	Laboratory investigation records and biological specimen banks based on an opportunistic collection	Laboratory investigation records based on an opportunistic collection	Vet and laboratory investigation records based on an opportunistic collection
Coverage of the population	97% and 77% respectively of public and private veterinary laboratories	59 laboratories in 52 departements	60 vets and laboratories
Duplication of data	Not controlled	Not controlled	Controlled
Target population	All animal productions, foodstuffs and environment	All animals sampled for an antibiogram	National poultry production
Study population	Strains from animals, foodstuffs and environment analysed by participating laboratories	Animals sampled for an antibiogram and analysed by the network partner laboratories (food animals and pets)	Poultry flocks traced by vets or laboratories
Epidemiological unit	Strain	Strain	Flock
Case definition	*Salmonella* strain identified in the sample	Strain isolated from an ill animal	Flock affected by a disease and notified by vets
Laboratory testing	Identification / Serotyping: laboratories and AFSSA AMR and PFGE: AFSSA	Identification / serotyping / AMR: participating laboratories	Identification / serotyping: participating laboratories
Data collection and management	AFSSA – LERQAP / CEB	AFSSA Lyon and Ploufragan	AFSSA Ploufragan
Analytical methodologies	Descriptive statistical analyses, unusual event detection	Descriptive statistical analyses + specific	Descriptive statistical analyses
Quality assurance	Quality assurance of LERQAP Accreditation for serotyping, Inter-laboratory trial for serotyping	Quality assurance of AFSSA laboratories, inter-laboratory trial for AMR testing	Standardization of poultry diseases diagnosis by common guidelines No analytical standardization
Bias	Willingness of the laboratories to participate Impact of regulation Investigator bias	Willingness of the laboratories to participate Detection bias Investigator bias	Willingness of the laboratories to participate Declaration bias Investigator bias Impact of the regulation
Reporting	Quarterly and annual reports to the network partners, unusual event reporting	Annual reports to the network partners	Bi-monthly and annual reports to the network partners

Table 4: Non-human passive surveillance in 2008