

ANNUAL  
REPORT



annoying  
nervous

# Summary

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## FOREWORD

# Open and active in the Greater Region

2018 has been a fantastic year for the LNS. There were so many highlights that it is impossible for us to mention them all in this foreword, even though all of them fully deserve to be recognised!

This year, LNS strengthened its position as a reference laboratory in Luxembourg and the Greater Region. In February Lydia Mutsch, the *ministre de la Santé*, Fernand Etgen, the *ministre de de l'Agriculture et de la Protection des consommateurs*, Reinhold Jost, the *Minister für Umwelt und Verbraucherschutz* in Saarland (Germany), and LNS ratified a memorandum of understanding in the field of analytical food control. LNS is also an essential contributor to three national health care plans orchestrated by the *ministère de la Santé*: the *Plan National Cancer* (National Cancer Plan), the *Plan National Antibiotiques* (National Antibiotic Plan) and the *Plan National Maladies Rares* (National Plan for Rare Diseases).

April and May were crucial months for the pathology and the genetic departments. In April, both received the mandate from the Government to operate as national diagnostic centres offering a comprehensive range of diagnostic and clinical activities in their respective disciplines. Within 1.5 years, the team from the National Center of Pathology (NCP) succeeded in reducing the primary outsourcing of Luxembourgish pathology cases to less than 0.1% by the end of 2018. Although the diagnostic turn-around times (TAT) have not yet reached their final objective, the NCP team achieved a significant reduction in the number of very long diagnostic TAT by September 2018. In May, the PEARL Scientific Advisory Board (SAB) meeting, in the presence of renowned experts in neuropathology and National Research Fund (FNR) representatives from Luxembourg, took place at LNS. It was a real success for the PEARL programme of neuropathology headed by Prof. Dr Michel Mittelbronn. The same month, the genetic department, now termed the National Center of Genetics (NCG), welcomed its new head, Dr Barbara Klink. Dr Klink is a human geneticist with an extensive expertise in clinical and tumour genetics. Previously she worked at

the Institute for Clinical Genetics, Medical Faculty Carl Gustave Carus at the Technische Universität Dresden where she also managed the Core Unit for Molecular Tumor Diagnostics at the German National Center for Tumor Diseases partner site.

In June, the *ministre de la Coopération et de l'Action humanitaire* Romain Schneider, in cooperation with LIH, signed the "Casamance Research-programme on HIV-Resistance and Sexual Health 2018-2022 agreement", otherwise known as CARES. Through operational research and capacity building, the CARES project will aim to improve access to diagnosis and treatment of HIV-infected people, thereby reducing HIV, HBV and HPV-related mortality in the region of Ziguinchor in Senegal (Casamance) and Guinea-Bissau. LNS is actively involved in the HPV component of CARES.

In July, the *ministre de la Justice*, Félix Braz, and the *ministre de la Santé*, Lydia Mutsch, officially inaugurated the unit for medicolegal documentation of injuries (umedo), which forms part of the department of forensic medicine. This new unit aims to offer, in collaboration with partner hospitals, to adult victims of physical and/or sexual violence free-of-charge documentation of injuries, thus securing evidence that can be used in legal proceedings at a later stage. This was a big step forward.

The same month Prof. Dr An Van Nieuwenhuyse, who is a specialist in occupational health medicine, was appointed as the new head of the department of health protection. She additionally holds a PhD in medical sciences and is guest professor in epidemiology at KULeuven. Previously she headed the Unit Health & Environment at the Belgian public health institute *Wetenschappelijk Instituut Volksgezondheid - Institut Scientifique de Santé Publique* (WIV-ISP). In addition, in that month, Mrs Alessandra Lanfranchi joined the LNS as the new lead of the human resources service.

LNS has also been very active in the academic field. Our staff members participated as speakers or visitors to international conferences and

workshops, published papers, organised meetings, and participated in several doctoral training programs supported by FNR, the Luxembourg National Research Fund. In March, Dr Ardashes Latsuzbaia and Joël Mossong, PhD, from the department of microbiology, published the first study on Human Papillomavirus vaccine update in Luxembourg in the journal *Vaccine*. In June, Dr Cosmin Florescu, from the National Center of Pathology, and Prof. Dr Friedrich Mühlischlegel were invited to a conference organised by Europa Donna Luxembourg – an international association supporting women and men in their fight against breast cancer - to talk about diagnostic activities of LNS related to breast cancer.

The presentation in August of our annual report 2017 in the presence of the *ministre de la Santé* Lydia Mutsch at a press conference and our event in November inviting all health professionals in Luxembourg were well received. They represented important steps towards greater visibility and openness of LNS. More institutions, and in particular international ones, increasingly become interested in our activities. For example, as part of a wider visit to research institutes in Luxembourg, we welcomed in September the visit of a delegation of scientists from the RIKEN Center for Integrative Medical Sciences in Yokohama, Japan.

We want to further widen our scope and give broader access to the information contained in our annual report and thus, as a team, decided to publish from now on our annual report in English.

As every year, LNS was involved in a raft of wonderful activities such as the "Lëtzt Go Gold" charity run of the *Fondatioun Kriibskrank Kanner*, the "Broschkriibslaf" organised by Europa Donna Luxembourg and the major patient solidarity event "Relais pour la Vie" by Fondation Cancer.

2018 also marks the end of the LNS 2016-2018 strategic plan. A new ambitious strategic plan (2019-2022) has been developed and we have no doubt that we will fully engage in this new plan over the next four years. Much has been achieved during the last year. We are deeply thankful to the LNS staff for carrying out their roles with such a high degree of commitment and professionalism. We would also like to take the opportunity to sincerely thank the former and current *ministre de la Santé* (Lydia Mutsch and Etienne Schneider) for their continuous support.

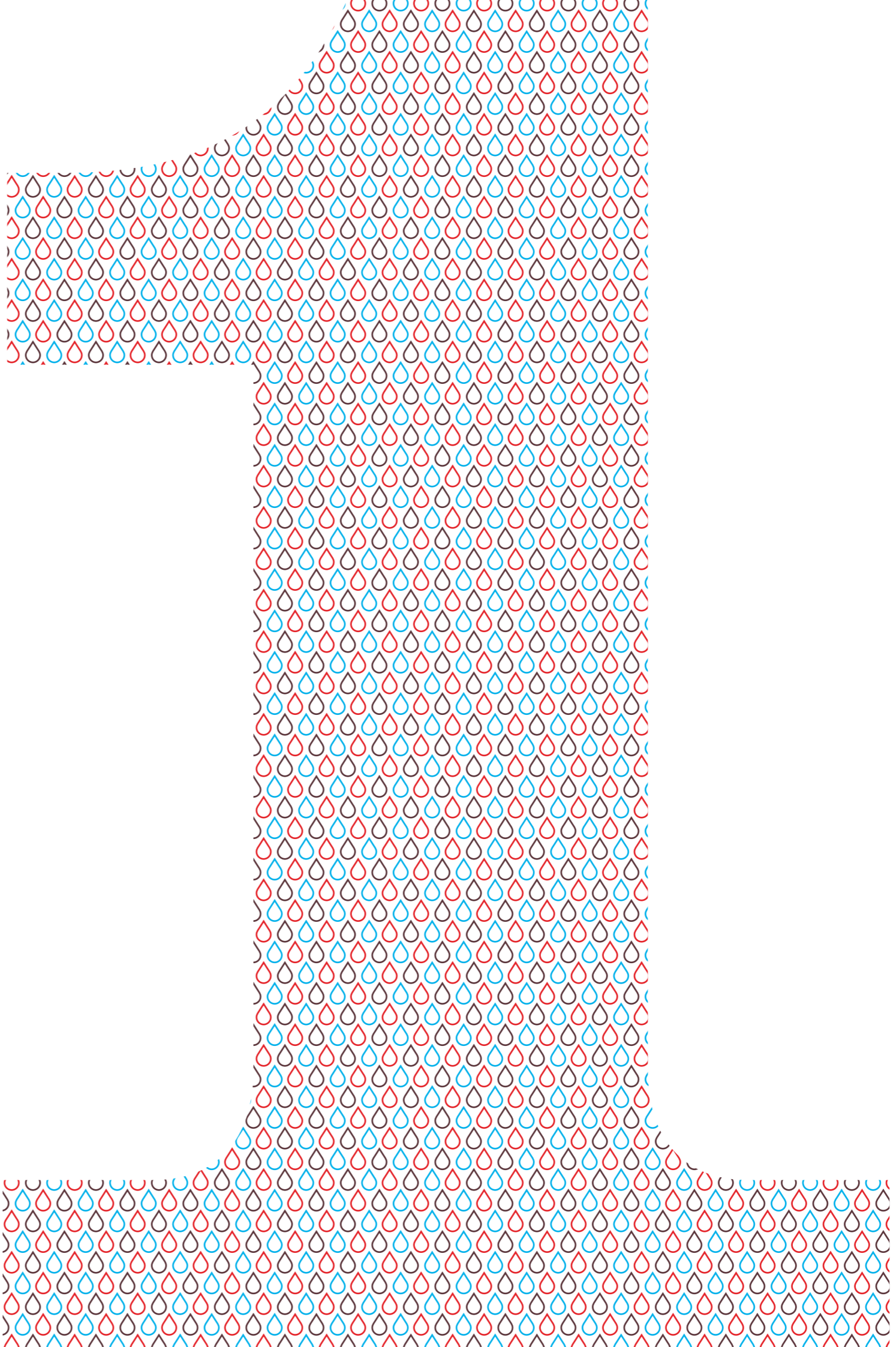
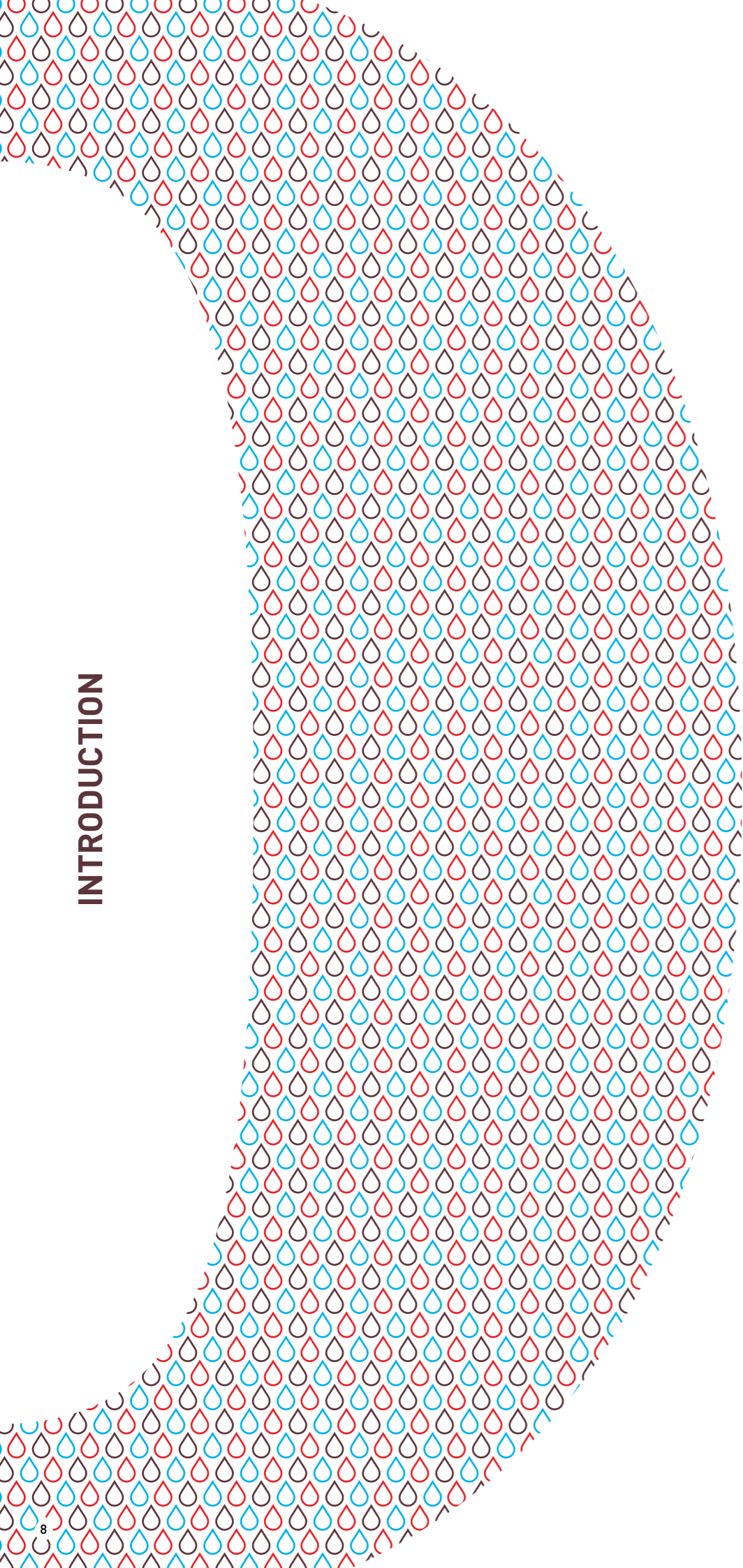


**Prof. Dr Simone P. NICLOU**  
President of the board



**Prof. Dr Friedrich MÜHLSCHLEGEL**  
Director

**INTRODUCTION**



## Governance bodies

The LNS is a public institution managed by the board of directors. The management of the laboratory is entrusted to a director assisted by the executive committee and a scientific council.

### BOARD OF DIRECTORS<sup>1</sup>

The LNS is under the control of the board of directors. It defines the general policy, organisation and functioning of the laboratory in compliance with applicable laws, regulations and conventions.

#### Members

##### Delegate from the *ministère de la Santé*

Prof. Dr Simone P. Niclou, president  
 Dr Jean-Claude Schmit, vice-president  
 Dr pharm. Cynthia Oxacelay  
 Mr Xavier Poos  
 Dr Marc Schlessler  
 Mrs Lucienne Thommes

##### Delegates from the *ministère de la Justice*

Mr Luc Reding  
 Mr Georges Oswald, advisory member

##### Delegate from the *ministère de la Recherche et de l'Enseignement Supérieur*

Mrs Josiane Entringer

##### Delegate from the *ministère de l'Economie*

Dr Françoise Liners

##### Delegate from the *ministère des Finances*

Mr Serge Hoffmann

##### LNS staff representative

Mr Frank Maas

### EXECUTIVE COMMITTEE

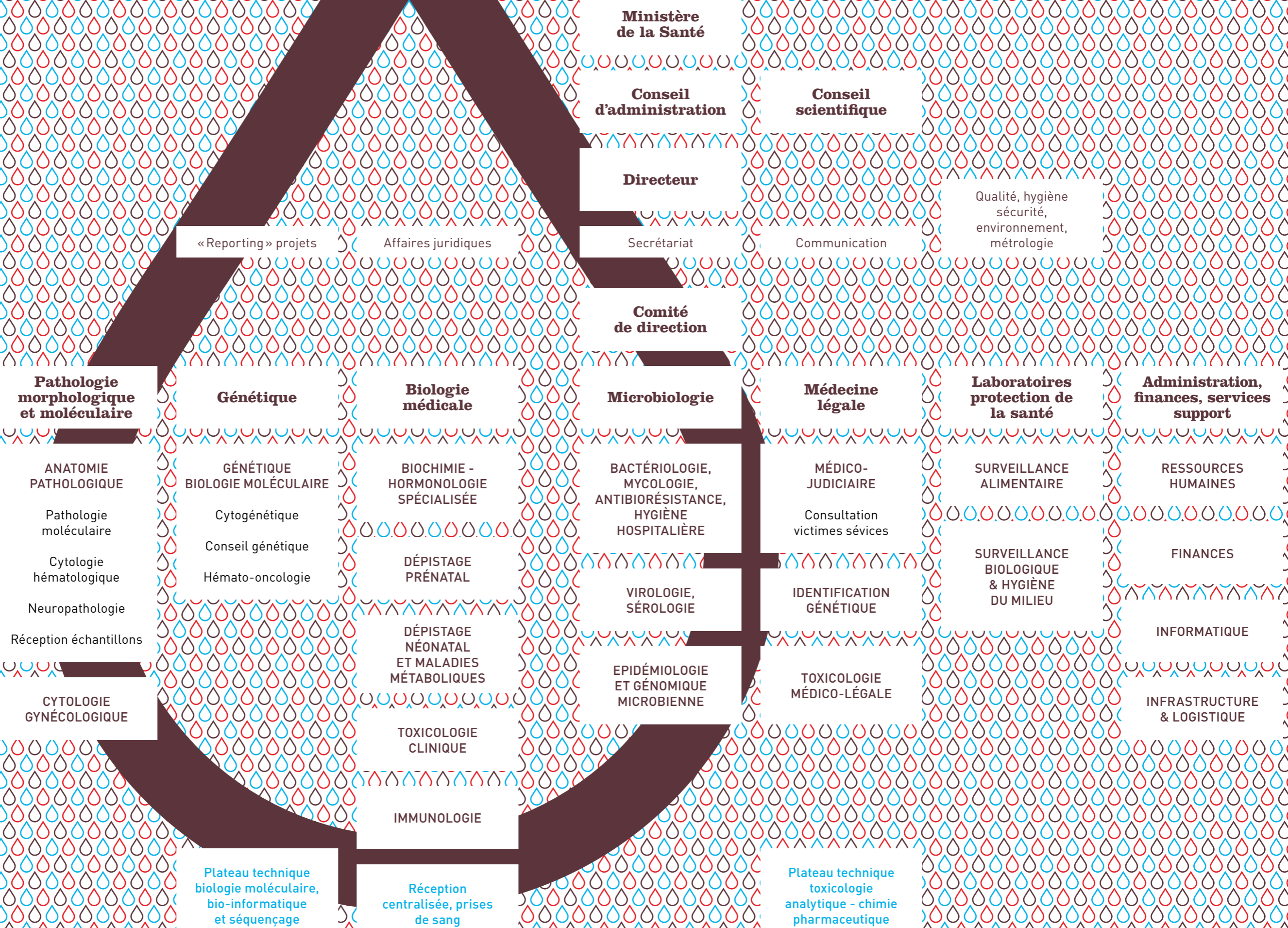
The executive committee, composed of the heads of department and lead by the director, meets at regular intervals to coordinate the activity of the institution.

### SCIENTIFIC ADVISORY BOARD

The scientific advisory board, composed of five members chosen among national and foreign experts, is responsible for contributing to the scientific agenda of the institution, expresses its opinion on the strategic plan and comments on the general guidelines for the activities of the laboratory.

The scientific advisory board gives its opinion on all matters falling within the area of competence of the institution.

<sup>1</sup>As at 31 December 2018.



\*Date of application: 01/01/2018



## 1. Staff

**265.5**

FULL-TIME  
EQUIVALENTS

**18**

NEW POSITIONS  
(excluding replacements)

**50**

NEW RECRUITS  
(fixed-term and permanent  
contracts)

**42.7**

AVERAGE AGE  
OF STAFF

**64.4%**

WOMEN

**35.6%**

MEN

**15**

NATIONALITIES

(Austria, Belgium, Brazil, Great Britain, France, Georgia,  
Germany, Hungary, Italy, Luxembourg, Netherlands,  
Portugal, Romania, Spain, Switzerland)

## 2. Total income

**51,068,966.6 €**



### 3. Activities department by department

MEDICAL BIOLOGY  
**101,640**  
BIOCHEMICAL ANALYSES

GENETICS  
**10,434**  
GENETIC ANALYSES

HEALTH PROTECTION  
**78,260**  
ENVIRONMENTAL HEALTH AND BIOLOGICAL MONITORING ANALYSES

**19,051**  
FOOD MONITORING ANALYSES

FORENSIC MEDICINE  
**9,026**  
GENETIC IDENTIFICATIONS

**3,441**  
EXPERTISE REQUESTS IN FORENSIC TOXICOLOGY

**147**  
FORENSIC MEDICAL AUTOPSIES AND EXPERT WITNESS REPORTS

**9,381**  
ANALYSES (technical platform for analytical toxicology and pharmaceutical chemistry)

MICROBIOLOGY  
**34,990**  
BACTERIOLOGY, MYCOLOGY AND ANTIBIOTIC RESISTANCE ANALYSE

**27,957**  
SEROLOGY ANALYSES

**15,123**  
PCR ANALYSES IN VIROLOGY

**86**  
CELL CULTURES

**9,742**  
MOLECULAR BIOLOGY ANALYSES

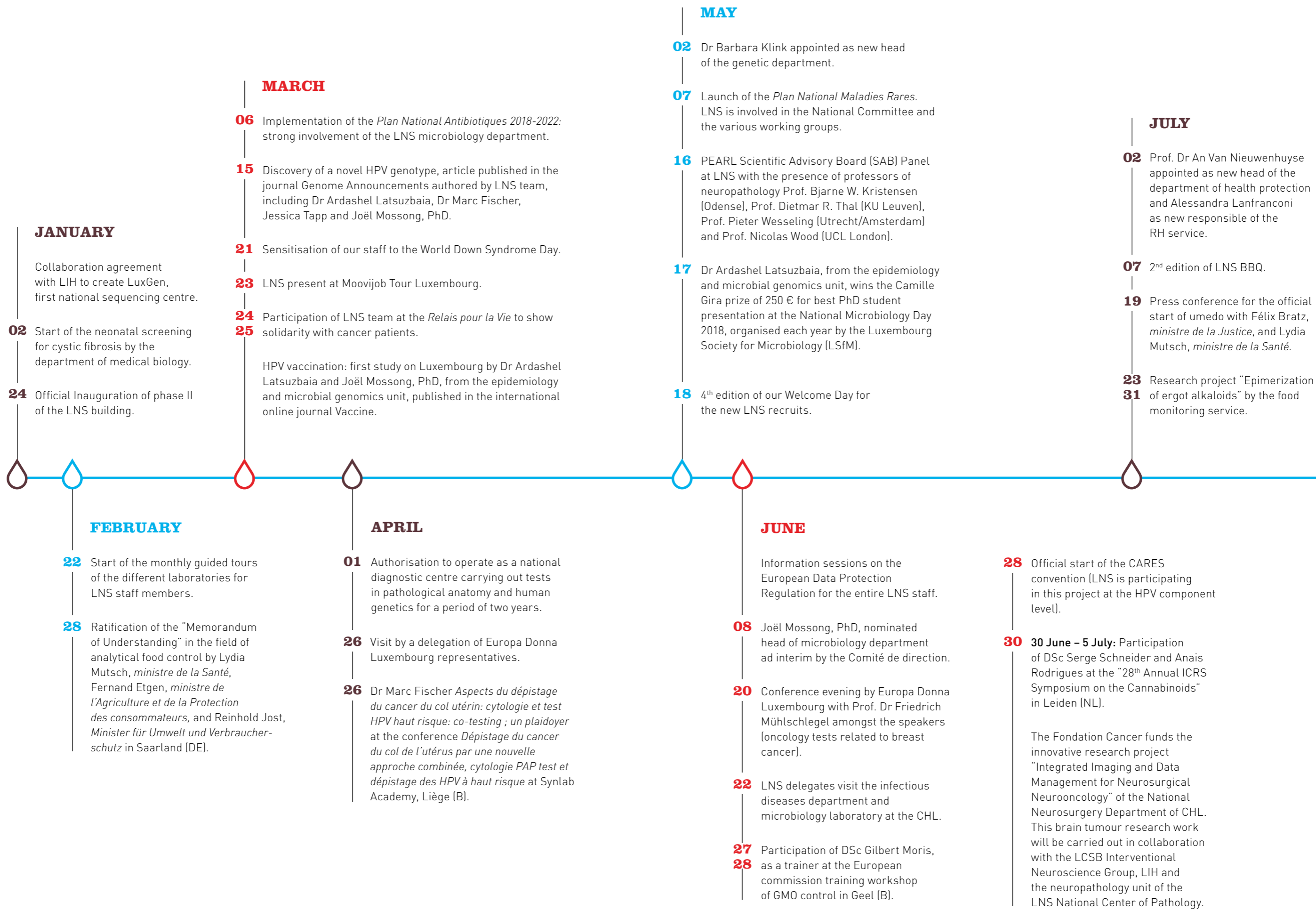
**1,400**  
WHOLE GENOME ANALYSES

ANATOMIC AND MOLECULAR PATHOLOGY  
**105,153**  
BIOPSIES, NON-GYNAECOLOGICAL SMEARS AND OPERATIVE SPECIMENS

**489**  
PCR ANALYSES IN HAEMATOLOGICAL CYTOLOGY, HAEMOSTASIS AND COAGULATION

**29**  
AUTOPSIES

**173,450**  
GYNAECOLOGICAL CYTOLOGY ANALYSES



## JANUARY

- Collaboration agreement with LIH to create LuxGen, first national sequencing centre.
- 02** Start of the neonatal screening for cystic fibrosis by the department of medical biology.
- 24** Official Inauguration of phase II of the LNS building.

## FEBRUARY

- 22** Start of the monthly guided tours of the different laboratories for LNS staff members.
- 28** Ratification of the "Memorandum of Understanding" in the field of analytical food control by Lydia Mutsch, *ministre de la Santé*, Fernand Etgen, *ministre de l'Agriculture et de la Protection des consommateurs*, and Reinhold Jost, *Minister für Umwelt und Verbraucherschutz* in Saarland (DE).

## MARCH

- 06** Implementation of the *Plan National Antibiotiques 2018-2022*: strong involvement of the LNS microbiology department.
- 15** Discovery of a novel HPV genotype, article published in the journal *Genome Announcements* authored by LNS team, including Dr Ardashes Latsuzbaia, Dr Marc Fischer, Jessica Tapp and Joël Mossong, PhD.
- 21** Sensitisation of our staff to the World Down Syndrome Day.
- 23** LNS present at Moovijob Tour Luxembourg.
- 24** Participation of LNS team at the *Relais pour la Vie* to show solidarity with cancer patients.
- 25** HPV vaccination: first study on Luxembourg by Dr Ardashes Latsuzbaia and Joël Mossong, PhD, from the epidemiology and microbial genomics unit, published in the international online journal *Vaccine*.

## APRIL

- 01** Authorisation to operate as a national diagnostic centre carrying out tests in pathological anatomy and human genetics for a period of two years.
- 26** Visit by a delegation of Europa Donna Luxembourg representatives.
- 26** Dr Marc Fischer *Aspects du dépistage du cancer du col utérin: cytologie et test HPV haut risque: co-testing ; un plaidoyer* at the conference *Dépistage du cancer du col de l'utérus par une nouvelle approche combinée, cytologie PAP test et dépistage des HPV à haut risque* at Synlab Academy, Liège (B).

## MAY

- 02** Dr Barbara Klink appointed as new head of the genetic department.
- 07** Launch of the *Plan National Maladies Rares*. LNS is involved in the National Committee and the various working groups.
- 16** PEARL Scientific Advisory Board (SAB) Panel at LNS with the presence of professors of neuropathology Prof. Bjarne W. Kristensen (Odense), Prof. Dietmar R. Thal (KU Leuven), Prof. Pieter Wesseling (Utrecht/Amsterdam) and Prof. Nicolas Wood (UCL London).
- 17** Dr Ardashes Latsuzbaia, from the epidemiology and microbial genomics unit, wins the Camille Gira prize of 250 € for best PhD student presentation at the National Microbiology Day 2018, organised each year by the Luxembourg Society for Microbiology (LSfM).
- 18** 4<sup>th</sup> edition of our Welcome Day for the new LNS recruits.

## JUNE

- Information sessions on the European Data Protection Regulation for the entire LNS staff.
- 08** Joël Mossong, PhD, nominated head of microbiology department ad interim by the Comité de direction.
- 20** Conference evening by Europa Donna Luxembourg with Prof. Dr Friedrich Mühlischlegel amongst the speakers (oncology tests related to breast cancer).
- 22** LNS delegates visit the infectious diseases department and microbiology laboratory at the CHL.
- 27** Participation of DSc Gilbert Moris, as a trainer at the European commission training workshop of GMO control in Geel (B).
- 28**

## JULY

- 02** Prof. Dr An Van Nieuwenhuyse appointed as new head of the department of health protection and Alessandra Lanfranchi as new responsible of the RH service.
- 07** 2<sup>nd</sup> edition of LNS BBQ.
- 19** Press conference for the official start of umedo with Félix Bratz, *ministre de la Justice*, and Lydia Mutsch, *ministre de la Santé*.
- 23** Research project "Epimerization of ergot alkaloids" by the food monitoring service.
- 31**

- 28** Official start of the CARES convention (LNS is participating in this project at the HPV component level).
  - 30** **30 June – 5 July:** Participation of DSc Serge Schneider and Anais Rodrigues at the "28<sup>th</sup> Annual ICRS Symposium on the Cannabinoids" in Leiden (NL).
- The Fondation Cancer funds the innovative research project "Integrated Imaging and Data Management for Neurosurgical Neurooncology" of the National Neurosurgery Department of CHL. This brain tumour research work will be carried out in collaboration with the LCSB Interventional Neuroscience Group, LIH and the neuropathology unit of the LNS National Center of Pathology.

## SEPTEMBER

- 01** Start of doctoral training unit "Microbiomes in One Health" funded by FNR and coordinated by LCSB: two PhD students and one postdoc will conduct research on this important topic at LNS over the next five years supervised by Joël Mossong, PhD, and Prof. Dr Friedrich Mühlischlegel.
- 04** Presentation by Dr pharm DSc Patricia Borde, head of the department of medical biology, of three clinical cases of metabolic diseases in Athens (GR) with CHL's neuropediatricians.
- 07**
- 26** Visit of a delegation of scientists from the Japanese RIKEN Center for Integrative Medical Sciences in Yokohama. The Japanese researchers came to Luxembourg as part of a joint symposium to consolidate links with LCSB, in collaboration with LIH, IBBL and LNS.

- 26** Participation of DSc Carole Dauberschmidt in EURL-NRL workshop on Pesticides in Almería (ES).
- 28**
- 29** Participation of some LNS staff members to the solidarity run "Lët'z Go Gold" organised by Fondatioun Kriibskrank Kanner.
- The ISO/CEI 17025: 2005 accreditation of the environmental hygiene and human biological monitoring service is maintained.

## NOVEMBER

- 07** Organisation of the first edition of the LNS health professional event.
- 12** Participation of Claude Marson, from the technical platform for analytical toxicology and pharmaceutical chemistry, at the CAP meeting of EDQM in Copenhagen (DK).
- 14**
- 13** Participation of Claude Schummer, from the food monitoring service, in EURL-NRL workshop on processing contaminants in Copenhagen (DK) and participation of Maud Servais, from the food monitoring service, in EURL-NRL workshop and training on pesticides in cereals in Copenhagen (DK).
- 15** Visit by members of the Planning familial.
- 15** **15 November – 19 December:** Participation of the umedo team at the Orange Week 2018 "Lët'z say no to violence against women".

- 19** Participation of Prof. Dr An Van Nieuwenhuysse, head of the department of health protection, as instructor in the H2020 project "Coordinating and advancing Human Biomonitoring in Europe to provide evidence for policy making" (HBM4EU), Radboud Medical University, Nijmegen (NL).
- 23**
- 20** The Hôpitaux Robert Schuman, in collaboration with the Centre National de Radiothérapie François Baclesse (CFB) and LNS, creates and successfully certifies a network of multidisciplinary specialist physicians for the diagnosis, management and follow-up of prostate cancer. This is the first oncological certification of its kind in Luxembourg for the most common human cancer. The certification is based on more than 120 criteria from the German Cancer Society [Deutsche Krebsgesellschaft - DKG].
- 30** 5th edition of our Welcome Day for the new LNS recruits.

## AUGUST

- 01** The food monitoring service classified as "A-lab" in an interlaboratory comparison test organised by the EU reference lab 'pesticides'.
- 09** **09 August – 06 September:** Exhibition *Ma vie continue / Mein Leben geht weiter* by the Fondation Cancer at LNS.
- 10** Presentation of the annual report 2017 in presence of Lydia Mutsch, *ministre de la Santé*, at a press conference.
- 16** Dr Thorsten Schwark, from the forensic medicine service, interviewed by RTL radio concerning the impact of insects in the elucidation of a murder.
- 22** Guided tour of the exhibition "Thierry! D'Expo" for interested LNS staff members.
- Provision of the EDUROAM network for the LNS staff.

## OCTOBER

- 02** Interview of Dr Monique Perrin, from the bacteriology, mycology, antibiotic resistance and hospital hygiene unit, about bacterial resistance published in Luxemburger Wort newspaper.
- 02** Participation at the 32<sup>nd</sup> papillomavirus international conference in Sydney (AU) of Joël Mossong, PhD, and Dr Ardashes Latsuzbaia, from the epidemiology and microbial genomics service.
- 06**
- 05** Interview of DSc Elizabet Petkovski, from the genetic identification service, about DNA tests published in the Paperjam newsletter.
- 06** Participation of an LNS team at the Broschtkriibslaf 2018, organised by Europa Donna Luxembourg.
- 14** Participation of Dr pharm. DSc Patricia Borde, head of the department of medical biology, at the 11<sup>th</sup> European meeting of the International Society of Neonatal Screening in Bratislava (SK), presenting the neonatal screening programme as carried out in Luxembourg. The next ISNS meeting will take place in Luxembourg in 2020, under the aegis of LNS.
- 17**

- 15** Participation of a team of LNS staff members at the "Pink Mob" organised by CHEM as part of Pink October.
- 17** Presentation by Joël Mossong, PhD, head ad interim of the of the department of microbiology, at the 19<sup>th</sup> meeting of National Focal Points for Microbiology at ECDC, Stockholm (SE), on the new legal framework for clinical laboratory reporting and for establishing public health microbiology reference laboratories in Luxembourg.
- 18** Meeting of the conseil scientifique:
- 19** Prof. Oliver Kurzai (Würzburg) visits and reports on the department of microbiology.
- 23** Oncopole-IUCT Luxembourg visit.
- Maintenance of the accreditation of the gynaecological cytology service.

## DECEMBER

- 01** Presentation of the department of health protection with an interview of our director Prof. Dr Friedrich Mühlischlegel published on 02 December by the newspaper Lëtzebuenger Journal.
- 14** IMI Conference in the premises of LNS with the intervention of Prof. Dr Friedrich Mühlischlegel about antibiotic resistance crisis.
- 14** LNS Christmas party with first ever appearance of the LNS music band.
- 14** Participation of DSc Serge Schneider at the "Table ronde PiPaPo" on the results of the PiPaPo project.
- 18** Dr Thorsten Schwark, from the forensic medicine service, is the guest of RTL Radio in the radio program "Am Gespräch".
- 20** Interview of DSc Elizabet Petkovski, from the genetic identification service, about paternity tests in the newspaper Le Jeudi.
- LNS staff members collect products as part of the *Action caritative du calendrier de l'Avent* to the benefit of the disadvantaged.

# 02



## Continuously improving personal data protection

On 25 May 2018, the General Data Protection Regulation (GDPR) came into effect. Citizens of the European Union now have greater control over their personal data and assurances that their information is being securely protected across Europe. According to the GDPR, personal data is any information related to a person such as a name, a photo, an email address, bank details, updates on social networking websites, location details, a computer IP address or medical information. As a multidisciplinary institute working in the health sector and having a massive amount of personal – and mainly sensitive – data, LNS must comply with the GDPR rules. According to Alice Xavier, lawyer at the LNS, the public institution took many initiatives to improve data protection long before the GDPR came into force.

*“ WE TOOK A LOT OF INITIATIVES LONG BEFORE THE GDPR CAME INTO FORCE AND WE ARE STILL WORKING TO IMPROVE PERSONAL DATA PROTECTION. ”*

**Alice Xavier**  
LNS lawyer





### RECORD OF DATA PROCESSING ACTIVITIES

“Already in 2017, our doctors were invited to an information session given by the CNPD (*Commission Nationale pour la Protection des Données*) regarding the basics and specific vocabulary of the data protection field”, explained Alice Xavier.

“We also initiated a three-step GDPR compliance process. The first step was to make a record of personal data processing activities by department as prescribed by article 30 of the GDPR (owner, short description, purpose, number of data subjects, categories of data subjects, categories of personal data). We organised about 15 workshops with LNS stakeholders, typically heads of department or other key representatives, and shared questionnaires to prepare for the meeting. Based on the information collected in the questionnaires and during the workshops, we identified the personal data processing activities and classified them according to their risks to establish priorities for the next steps. The results were reviewed and validated by LNS stakeholders.”

### GDPR HIGH-LEVEL ASSESSMENT AND RECOMMENDATIONS

The second step was to identify high-level gaps with key requirements of the GDPR (e.g., existence of specific policies and procedures, privacy considerations, data management, etc.). “A series of workshops with the LNS stakeholders in charge of legal, compliance and IT – including security – functions enabled us to create a matrix containing the list of key requirement areas from the GDPR with the high-level status of fulfilment at LNS – met, partially met or not met – and the corresponding gaps”, said Alice Xavier. “We then proposed an action plan with practical recommendations grouped by priorities and based on lessons learned, healthcare industry and best practices as well as a roadmap for implementing these recommendations. The results of the workshops, the GDPR matrix, the recommendations and the roadmap were summarised in a final report.”

### APPOINTMENT OF A DATA PROTECTION OFFICER

“After the validation of the report, we appointed an external data protection officer (DPO) to help us carry out the recommendations and to address the most critical risks before the entry into force of the GDPR”, added Alice Xavier. “2018 was a crucial year to put in place governance and accountability measures, including presenting the recommendations and first steps of the DPO at the board, defining high-level procedures, describing the roles and responsibilities within LNS and setting up staff training sessions in French, English and German. These sessions aimed to ensure that each staff member has the same level of understanding of the GDPR rules (what is a personal data, what are the rights of patients<sup>1</sup>, what to do in case of data breach, etc.), is aware of their individual responsibility for data protection and will apply high-level procedures efficiently.”

“For 2019, our main targets will be hiring an internal DPO, further strengthening our cybersecurity environment and going in deep with more technical procedures”, concluded Alice Xavier. “Data protection compliance is constant teamwork.”

<sup>1</sup> Under the GDPR, individuals have 8 basic rights: the right to access, the right to be forgotten, the right to data portability, the right to be informed, the right to have information corrected, the right to restrict processing, the right to object, the right to be notified.



## Legal

### ACTIVITIES

- Participation since November 2018 in the ELIXIR working group composed of data protection professionals. The aim of this working group is to find a common understanding within the field of research, for example the definition of controller/processor, the best practices for information sheets and consent forms, the interpretation and limitations of further processing for research, etc.
- Coordination of legal reviews of various specifications to be published in the context of the public procurement procedure. Legal support to the investment committee for the interpretation of the new law on public procurement (Law of 8 April 2018 on public procurement and its implementing regulations).

## Communication

### ACTIVITIES

- Welcome drink for LNS, IBBL and LMV staff members to get to know each other.
- Official inauguration of phase II of the building.
- Lunch with the staff members celebrating an anniversary.
- Summer barbecue for the staff and their families.
- Cultural visit to the exhibition "Thierry! D'EXPO" in Dudelange with interested staff members.
- Christmas party for LNS staff.
- First edition of an evening dedicated to the health professionals at the LNS.
- LNS presence at Relais pour la Vie, LëtZGoGold and Broschkriibslaf.
- 2 editions of the Welcome Days, in collaboration with HR, for new recruits.
- Exhibition *Ma vie continue/Mein Leben geht weiter*.
- Guided tours for groups.
- 8 videos presenting different aspects of LNS through the eyes of LNS staff members as well as a video presenting the outsides of the LNS building.
- Change management project to define the vision and values of LNS.
- Supervision of the series "20" from the administration" presenting administrative topics at regular intervals to the LNS staff.
- LNS teams at ING Night Marathon, Leopard UTML Ultratrail du Müllerthal, ING Route du Vin, Trail Uewersauer.
- Regular updates of the LNS intranet with articles and other interesting topics for the staff.
- Press relations.

## Quality, Safety/ Environment and Hygiene, Metrology (QHSEM)

### ACTIVITIES

#### Metrology

- Acquisition of a 6-digit balance for the internalisation of pipettes metrology.
- New metrology assistance tool: register (tickets) and follow-up of lab requests.

#### Quality

- Linking of QHSEM unit to General Management.
- Strengthening the team with the hiring of a quality assistant.

#### Security

- Strengthening first aid resources and skills.
- Complete reorganisation of building access.
- Validation by an external audit of the new fire coordination procedure.

## Operational reporting

### ACTIVITIES

- The LNS strategic plan 2016-2018 counts 233 operational objectives for which 157 have been accomplished at the end of December 2018 with a success rate going from 75% to 100%. A detailed status overview for all operational objectives per department has been established in a final report.
- A new four-year strategic plan 2019-2022 presents itself as a more comprehensive, more flexible and more team-based endeavour, thus creating a meaningful and robust platform from which to achieve the identified goals. The new plan rejoins the former one by providing key strategies, which focus on the different elements of the LNS vision and, when applied, translate this vision into reality. Specific departmental objectives are defined for all common key strategies and, when compared to the former plan, will be managed in a more adapted and fluid way over time.
- The unit is taking over responsibility for implementing the requirements regarding the law of 14 September 2018 on a transparent and open administration at LNS. First public data are made electronically available.
- At the end of 2018, LNS has published 47 scientific papers relating to its departmental research topics.

# LNS

DEPARTMENT  
OF FORENSIC MEDICINE



## Using new technologies to complement the work of forensic pathologists

The forensic medical service covers several areas of responsibility. Most commonly known are forensic autopsies, which help to establish the cause of death and contribute to police investigations. In certain autopsy cases, medical imaging can be of particular benefit in the context of these examinations. However, conventional radiographs of bodies have always been part of the routine catalogue of procedures performed at LNS. Since January 2018, a collaboration with the *Centre Hospitalier de Luxembourg* (CHL) gives the forensic experts access to a highly performant computed tomography (CT) scanner and a highly experienced team of radiologists and imaging-technologists. The use of this new generation of CT scanners for pre-autopsy examinations opens new perspectives in the forensic casework.

*"POST-MORTEM CT IS A VALUABLE ADDITION TO OUR ROUTINE WORK AND THE COLLABORATION BETWEEN LNS AND CHL ENABLES US TO COMPLY WITH INTERNATIONAL STANDARDS."*

**Martine Schaul**  
Specialised in legal medicine





"We conduct about 100 autopsies per year by order of the investigating magistrates", explained Martine Schaul, one of the three forensic pathologists of the service. "Depending on the circumstances of the case, we determine whether a post-mortem CT of the body before an autopsy is indicated – this is the case in approximately 30% of all autopsies. Once the investigating judge requests imaging, based on our advice, the corpse is transferred into an additional body bag and transported to CHL where the CT scan is carried out; a whole-body CT scan takes only a few minutes. We then discuss the results with the radiologists of the CHL. In 2018, we conducted 27 post-mortem CT scans ahead of autopsies."

#### A MORE ACCURATE TECHNOLOGY

"The plain X-rays, which we can perform at the LNS, only allow a two-dimensional view and are often not easy to interpret", commented Martine Schaul. "In order to detect the exact localisation of foreign bodies, such as bullets, we have to take images from different angles and sometimes we have to reposition the corpse. Thanks to post-mortem CT (PMCT), bullets for example are visualised in their exact relation to anatomic structures. Based on that information, we can focus on the dissection and retrieve such foreign bodies carefully without damaging them. Furthermore, the CT data documenting the state of the entire body prior to the autopsy are archived and can be accessed at a later time if new questions or clues emerge during the ongoing investigation. The data could even be reassessed by other experts, even if the body had been cremated in the meantime."

Based on these data and by using software tools, the forensic pathologists of the service, together with the cooperating radiologist, can reconstruct relevant fractures and demonstrate them in 'clean and neutral' images, or even print a copy of relevant osseous injuries with 3D-impression technology. Those printouts can then be taken into the courtroom to illustrate the conclusions drawn by forensic pathologists.

#### A COMPLEMENTARY METHOD TO THE AUTOPSY

"The CT scanning has many advantages when compared to autopsy", emphasized Martine Schaul. "While some parts of the skeleton are difficult to access at autopsy, CT scanning visualises every single bone from head to toes. If the bones show no pathological findings in the CT, we generally do not go beyond the usual extent of the autopsy. This allows us to preserve the body as best as possible for the family. Documenting bone injuries in the original state often provides a better overview of the fractures because the subsequent dissection at autopsy may cause a disjunction of the fragments. Besides the advantages in detecting bone injuries and foreign bodies, PMCT can reliably diagnose gas and fluid accumulations and may show singular anatomical traits or implants allowing for identification of an unknown corpse. Furthermore, measurements of a bullet path or a stab wound are often more accurate in CT scans due to the integrity of the body".

"Post-mortem CT technology will not replace autopsy", concluded Martine Schaul. "Both methods are complementary. Each one adds valuable information to the other."



## Technical platform for analytical toxicology and pharmaceutical chemistry

### RESEARCH PROJECTS

Launch of a project to analyse medicines seized by customs at Luxembourg airport. Several hundred pharmaceuticals and food supplements, mainly from India and China, are seized each year because they do not have a marketing authorisation in the Grand Duchy. The samples are analysed in collaboration with the ministère de la Santé for their pharmacological quality (purity, concentration of the pharmacological product, presence of synthetic contaminants, etc.).

### ACCREDITATION

Certification and accreditation according to standard 17025 in progress.

**1,202**

PHARMACEUTICAL CHEMISTRY ANALYSES

**8,179**

ANALYTICAL TOXICOLOGY ANALYSES

**9,381**

TOTAL NUMBER OF ANALYSES

## Forensic toxicology

### ACTIVITIES

- Significant increase in hair analysis in 2018 compared to 2017: +38% due, among other things, to an influx of samples from Belgium for the determination of a specific marker for cannabis consumption in hair (THC-COOH).
- Various studies were carried out during internships by students and scientists:
  - > Influence of thermal hair straightening on cocaine positive hair and evidence after heat treatment of anhydroecgonine méthylester cocaine (AEME), known to be a specific marker for crack use.
  - > Development of an optimised method for the determination of GHB (gamma-hydroxybutyric acid) in hair and study of the correlation between capillary GHB and the doses consumed (carried out in collaboration with the University of Antwerp).
  - > Determination of the concentration zone of CBD, THC and CBN in hair of people consuming hemp extracts containing CBD (study carried out in collaboration with the analytical toxicology service).
  - > Influence of hair colouring, bleaching and chemical curling on different cannabinoids in hair.
  - > Development of a specific blood marker for alcohol consumption: phosphatidylethanol (PEth).

**855**

SAMPLES FROM AUTOPSIES

**465**

SAMPLES FOR URINARY ETG ANALYSES

**217**

BAC ANALYSES

**1,293**

HAIR SAMPLES

**611**

SAMPLES OF LEGAL CASES ON LIVING ORGANISMS

## Forensic medical

### ACTIVITIES

Official launch of the unit for medicolegal documentation of injuries, umedo, with 11 cases in 2018 (July – December 2018)

**95**

AUTOPSIES

(in 27 cases a post-mortem computed tomography was performed)

**52**

EXPERT WITNESS REPORTS

## Genetic identification

### ACTIVITIES

- In order to meet the growing demands, the service strengthened its workforce by hiring two additional employees in March 2018, including a senior expert. The number of expert casework carried out was 24% higher and the total of samples processed increased by 37% compared to the previous year.
- In addition to its expertise, the service continued to ensure quality standards, technical accuracy and availability and maintained its accreditation under the ISO 17025 standard.
- The cooperation with the judicial police service of the Grand Duchy Police Force continued to be highly successful, allowing fruitful collaboration as well as pooling of specific knowledge.
- In close collaboration with the forensic medical service, the service was also involved in an international project on age estimation by DNA methylation analysis.

**1,871**

EXPERT REPORTS

**10,492**

SAMPLES



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NATIONAL CENTER  
OF PATHOLOGY

## DNA methylation classification: a powerful tool to improve tumour diagnoses

The department of anatomic and molecular pathology, now the National Center of Pathology (NCP) since 1 April 2018, is the largest department in the LNS. It is involved in the care of a large patient population, analysing more than 180'000 samples per year and is divided into two divisions: gynaecological cytology and anatomic and molecular pathology.

*"BY CLASSIFYING TUMOURS  
ACCORDING TO THEIR EPIGENETIC  
SIGNATURE, WE CAN CLASSIFY  
THEM MORE ACCURATELY."*

**Prof. Dr Michel Mittelbronn**  
Neuropathologist  
(FNR) PEARL Chair in neuropathology  
Head of National Center of Pathology



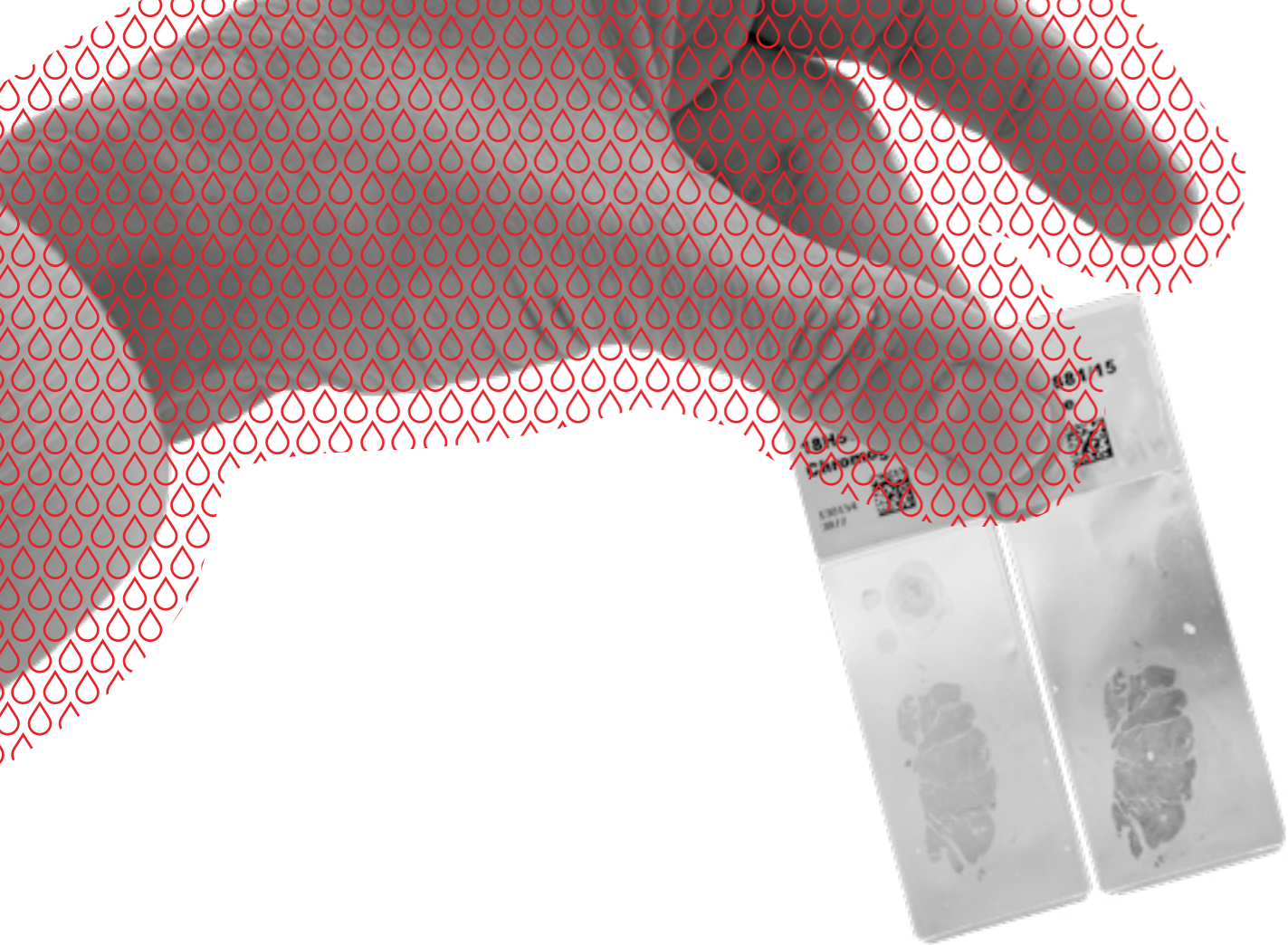


### 10 TO 15% OF IMPRECISE DIAGNOSES WITH STANDARD METHODS

The National Center of Pathology is increasingly involved in the establishment of new techniques and new molecular tests such as DNA methylation-based classification of tumours. Based on epigenetic biomarkers, this new method improves tumour diagnoses significantly. "While traditional genetics explains the way the DNA sequences are passed on from one generation to the next, epigenetics describes how genes are regulated in different cell types", commented Prof. Dr Michel Mittelbronn, head of the NCP. "We know that a part of how epigenetics work is by adding and removing chemical tags to DNA. These tags highlight particular genes with information whether they should be switched on or off. They are called methyl groups<sup>1</sup> and are used to modify one of the four chemical bases adenine (A), guanine (G), cytosine (C) and thymine (T) that make up the genetic code of our DNA. The base usually tagged with a methyl group is cytosine. When cytosine is methylated, the DNA maintains the same sequence, but the expression of methylated genes can be considerably different. Since a few years, we have discovered that DNA methylation is quite stable in different tumour entities and that many tumours have their own specific epigenetic methylation profile. By classifying tumours according to their epigenetic signature, we can classify them more accurately."

According to Prof. Dr Michel Mittelbronn, this new tool can change a diagnosis in up to 15% of prospective cases. "With the standard methods such as the microscopic analysis, we, as neuropathologists, probably classified between 10 and 15% of all tumours in an imprecise manner. These imprecise diagnoses are not related to a lack of knowledge but might be related to multiple reasons. The tissue may be difficult to access or a large resection would be too invasive and therefore dangerous for the patient. In addition, pathologists are usually making a subjective interpretation of the microscopic image which might be prone to subjective biases. For example, we frequently have to diagnose cases with the question if a tumour is benign or rather malignant. At first glance, some tumours appear morphologically benign and would therefore not require particular additional treatment. However, sometimes the epigenetic signature indicates a highly malignant tumour such as glioblastoma, one of the most aggressive brain cancers that has to be treated rapidly with chemotherapy and radiotherapy."

<sup>1</sup>Methyl groups are one of the commonest structural units of organic compounds. They consist of a carbon atom surrounded by three hydrogen atoms, expressed as CH<sub>3</sub>.



## THE POTENTIAL TO TRANSFORM TUMOUR PATHOLOGY

"You can compare the epigenetic signature of a tumour to the ID card of a person. Even if persons are disguised, we are able to recognise them by their ID number. It is the same logic with the DNA methylation-based classification. This powerful tool allows us to make more precise and more unbiased diagnoses, especially in neuropathology and probably also for soft and bone tissues tumours, and to better stratify patients according to treatment strategies."

"To determine the DNA methylation patterns in samples, we are first applying a bisulphite treatment", continued Prof. Dr Michel Mittelbronn. "When cytosine is methylated, the bisulphite treatment doesn't change the methylation and leaves cytosine residues unaffected. In contrast, when cytosine is unmethylated, the bisulphite

treatment converts the cytosine residues to uracil, one of the four bases in the nucleic acid of RNA. Afterwards, bisulphite converted DNA samples are amplified, fragmented and hybridised to chips that are then scanned by a laser-based, high-resolution optical imaging system. To make it simple, this array scanner, which can read hundreds of thousands of methylation sites very accurately, allows us to calculate the percentage of methylation according to the presence or absence of uracil in each patient DNA. This presence or absence of uracil is highlighted in different colours."

"And it is just the beginning", concluded Prof. Dr Mittelbronn. "This DNA methylation classification has the potential to fundamentally transform tumour pathology thanks to the next generation of machine-learning-based tumour classifiers."



## Gynaecological cytology

### ACTIVITIES

- Maintenance of the ISO15189 accreditation.
- Lectures by Dr Marc Fischer, responsible of the service:
  1. "Aspects du dépistage du cancer du col utérin : cytoplogie et test HPV haut risque : co-testing ; un plaidoyer" at the Dépistage du cancer du col de l'utérus par une nouvelle approche combinée, cytoplogie PAP test et dépistage des HPV à haut risque conference at Synlab Academy in Liège (B), 26/4/2018.
  2. "From conventional cytology to LBC with HPV testing: cervical screening in Luxembourg" at the European Congress of Cytology, Hologic satellite symposium in Madrid (ES), 12/06/2018.
  3. Wechsel von konventioneller Zytologie zur Dünnschichtzytologie mit HPV-Testung: ein Erfahrungsbericht aus Luxemburg. At the Qualitative Verbesserung des Zervixkarzinom-Screenings symposium by Fachgruppensitzung Pathologie in Vienna (AT), 10/10/2018.

**123,120**

**CERVICAL-VAGINAL SMEARS**  
(in liquid-based chromatography and conventional)

**27,353**

**MOLECULAR BIOLOGY ANALYSES: HUMAN PAPILLOMAVIRUS (HPV-HR) DETECTION**

**4,978**

**MOLECULAR BIOLOGY ANALYSES: HUMAN PAPILLOMAVIRUS (HPV-GT) GENOTYPING**

**12,233**

**MOLECULAR BIOLOGY ANALYSES: CHLAMYDIAE TRACHOMATIS AND NEISSERIA GONORRHAEE (combined test: COMBO 2)**

**5,766**

**MOLECULAR BIOLOGY ANALYSES: MYCOPLASMA GENITALIUM (MGEN)**

**173,450**

**TOTAL NUMBER OF ANALYSES**

## Pathological anatomy

### ACTIVITIES

- Telepathology project established at all 4 hospital sites (CHEM, CHL, CHdN, HRS).
- 19 publications in 2018 (among those Nature (IF: 41.5); Autophagy (IF: 11.1); Embo Molecular Medicine (IF: 10.3)).
- Set up of a technical secretariat/project management.
- Nomination of a quality manager and deputy.
- Set up of the electronic report transmission (CHL, HRS) together with IT/Dep Admin/Finance.
- Participation of the Prostate Center HRS (ONKOZERT).
- New LSM confocal microscope.
- Installation of an epigenetic platform.

**101,153**

**BIOPSIES, NON-GYNAECOLOGICAL SMEARS AND OPERATIVE SPECIMENS**

**489**

**ANALYSES IN HAEMATOLOGICAL CYTOLOGY, HAEMOSTASIS AND COAGULATION**

**29**

**CLINICAL AUTOPSIES**



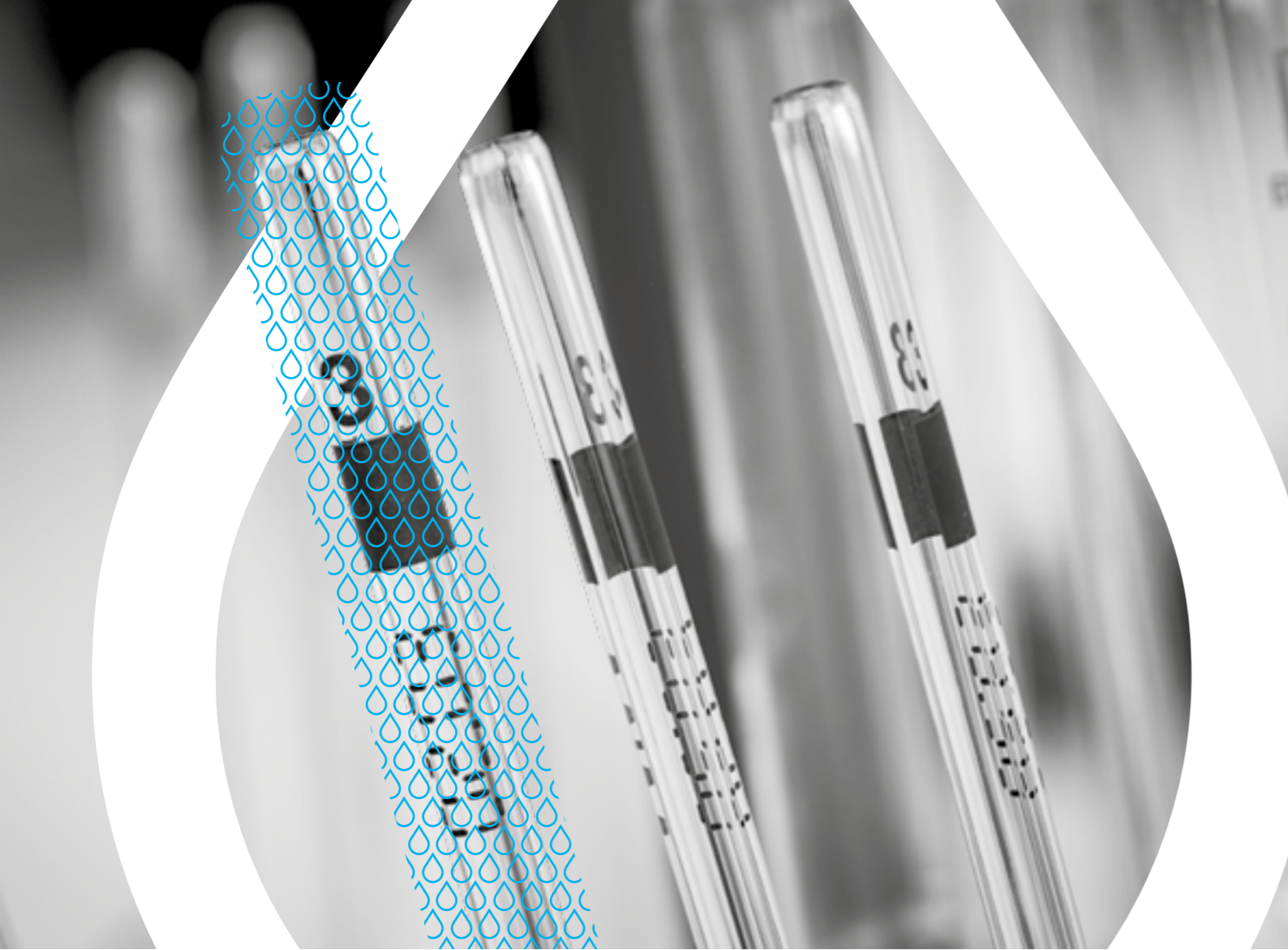
## Detecting natural contaminants in food

The food monitoring service is one of the two units of the department of health protection. Its activities consist in performing chemical, biochemical and microbiological analysis of food, feed and seed that have been collected by the various authorities involved in the official control of the food chain. One of its essential missions is to detect and analyse contaminants in food. Contrary to what one might think, food and beverages are not only contaminated with agricultural, environmental or industrial sources (pesticides, nitrates, additives, plasticizers, heavy metals, PCB, dioxins, process contaminants such as polycyclic aromatic hydrocarbons, nitrosamines, acrylamide). There are also natural food contaminants produced by other living organisms: bacteria, fungi and some plants.

*"THE FOOD CONTAMINANTS ARE NOT ONLY RELATED TO HUMAN ACTIVITIES. THERE ARE ALSO NATURAL CONTAMINANTS PRODUCED BY OTHER LIVING ORGANISMS."*

**DSc Gilbert Moris**  
Head of the food monitoring service





### **BACILLUS CEREUS, A UBIQUITOUS HUMAN PATHOGEN**

"Bacteria such as *Bacillus cereus* are widely distributed environmentally", stated DSc Gilbert Moris, head of the food monitoring service. "This type of bacteria produces toxins that can cause two types of illness: one characterised by diarrhea and the other, called emetic toxin, by nausea and vomiting. They are present in a variety of foods, particularly rice and leftovers, as well as sauces, soups and other prepared foods and can quickly multiply at room temperature. We have different methods to detect them. First, we use an agar medium. After having prepared a mother suspension of the sample to be analysed according to a ratio of 10 (1 part solute + 9 parts diluent for a total of 10 parts), we put 1% of it into a medium containing the gelling agent agar-agar, a chromogenic substrate which colourises the *Bacillus cereus* bacteria, and antibiotics which inhibits the growth of other bacteria. After one or two days of incubation, the *Bacillus cereus* bacteria appear in the form of colonies with a characteristic green colouration. Another method based on molecular biology is the polymerase chain reaction (PCR), a technique used to make many copies of a specific DNA region *in vitro* (in a tube rather than in an organism). The purpose is to detect the presence of the gene that produces the toxin and to evaluate the percentage of bacteria that have this genetic sequence and will express it."

### **THE TOXIC EFFECTS OF MYCOTOXINS**

Certain fungi (moulds) can also have a negative impact on human health by infecting agricultural commodities in the field and/or during storage and producing mycotoxins. The occurrence of these toxic metabolites on grains and animal food susceptible to mould infestation is influenced by environmental factors such as temperature, humidity levels, and/or rainfall during growing, harvesting and post-harvesting. When an outbreak occurs, mycotoxins are produced in food commodities, some of which are used in animal food. The mycotoxins will then remain in the food throughout every phase of food production. Mycotoxins are tough to expel from food and are not destroyed by most of the processes used in animal food production. When consumed by animals or humans, the results can be detrimental causing toxicity or even death. Mycotoxins may cause various toxicological problems such as neurological issues, liver failure, kidney failure, and cardiac failure.

"*Aspergillus*, *Penicillium* and *Fusarium* are the most common mycotoxin-producing genera", explained DSc Gilbert Moris. "*Aspergilli* are mostly present in (sub-) tropical regions and mainly affect cereals, nuts and spices. They produce mycotoxins that may have a serious impact on the health of humans and animals such as aflatoxins, sterigmatocystins and ochratoxins. Aflatoxin B1 is the most hepatotoxic and hepatocarcinogenic of the aflatoxins produced by *Aspergillus* species. *Penicillium* species are prevalent in cereals, apples and coffee. For instance, *Penicillium expansum* produces patulin, a toxin that causes neurotoxic, immunotoxic and gastrointestinal effects in animals and is potential genotoxic for humans. *Fusarium* moulds cause diseases of many economically important crop plants (wheat, barley oats, etc.) in our countries. Some species are known to colonise stored cereal grains not only causing losses but also producing mycotoxins that are harmful to humans and animals."

Ultra-high-performance liquid chromatography coupled with tandem mass spectrometry (UPLC-MS/MS) is mainly used to detect mycotoxins. This analytical technique combines the physical separation capabilities of liquid chromatography with the mass analysis capabilities of mass spectrometry and can identify several mycotoxins at the same time.

### **SAFETY ISSUES AFFECTING HERBS: PYRROLIZIDINE ALKALOIDS**

Some plants also produce toxins, in particular pyrrolizidine alkaloids (PAs). Many of these are weeds that can grow in fields and contaminate food crops. PAs can be acutely toxic and some of them have a DNA-damaging potential that may lead to cancer. PAs are stable during processing and have been detected in herbal teas, honey, herbs, spices and other food products such as cereals. "Due to the complexity of the subject and a large number of related compounds, the overall health risk has not been fully evaluated yet", remarked DSc Gilbert Moris. "There are several hundreds of molecules, which are all alike but all different. The European Food Safety Authority (EFSA) has selected 20 in food and feed that we are supposed to identify. We use the same detection method as for mycotoxins, but UPLC-MS/MS is not yet fully implemented. The EFSA must still set the limit of quantification".





## Food monitoring

### ACTIVITIES

- Accreditation of two new methods, including one for the analysis of the ergot alkaloids in cereal-based food and feed, and one for the analysis of azo dyes in spices. The accreditation and routine application of the ergot (alkaloids) analysis method, together with tests for the implementation of a method for the study of pyrrolizidine alkaloids, is a first step for the laboratory towards the new techniques required by the European Reference Laboratory for mycotoxins and plant toxins. It also helps the laboratory to consolidate its role as the national reference laboratory in this field. In addition, the analysis of ergot alkaloids from rye is a highly requested method of ASTA, for which the laboratory has analysed about thirty animal feeds.
- Start of the laboratory's collaboration with the *Landesamt für Verbraucherschutz* in Saarbrücken.

In this context, the laboratory analysed 60 samples for the presence of mycotoxins, furans and azo dyes.

- In terms of microbiological analyses, the laboratory has intensified its collaboration with the *Laboratoire de médecine vétérinaire de l'Etat* (LMVE), mainly through joint participation in interlaboratory tests organised as part of our status as a national reference laboratory for Salmonella and enterohaemorrhagic *E. coli* (EHEC). In the case of EHECs, the laboratory has been able to expand its detection range to 13 serotypes, following the requirements of the European Reference Laboratory.
- Concerning GMO detection, the laboratory has also continued to expand its detection range to cover all new GMOs for which an authorisation file has been submitted to the European Commission.

**14,475**

MICROBIOLOGICAL ANALYSES

**205**

ANALYSES CONCERNING THE PRESENCE OF GMOs

**4,371**

ANALYSES CONCERNING THE PRESENCE OF PESTICIDES, CONTAMINANTS OR OTHER ADDITIVES

**19,051**

TOTAL NUMBER OF ANALYSES

## Environmental hygiene and human biological monitoring

### ACTIVITIES

- The service has further expanded its activities in the field of indoor pollution, by assisting the *ministère de la Santé* also in the field sampling in private houses, schools, day-care facilities...
- For the market consumer products, the service became accredited ISO 17 025 for the analyses of nickel in jewellery.
- For the control and monitoring of heavy metals in food, the service has continued its analyses in food and food contact materials, and has obtained the approval for the necessary equipment to develop speciation analyses in the future.
- Concerning human biomonitoring (HBM), LNS has joined the H2020 European initiative 'HBM4EU, "Coordinating and advancing human biomonitoring in Europe to provide evidence for chemical policy making" and the service has been accepted as participant in the large-scale European inter-laboratory tests for HBM of metals.
- The service is ISO 17 025 accredited. For the HBM activities, it was decided to stop the ISO 17 025 accreditation in March 2018 and prioritise the development of the ISO 15 189 required for reimbursement of this type of analysis in Luxembourg. To this purpose, the department of health protection and the department of medical biology have created a common platform. In the mid-long term, HBM analyses will be accredited again ISO 17 025, this in line with the strategy at the European level.

**62,895**

ENVIRONMENTAL HEALTH ANALYSES

**15,365**

BIOLOGICAL MONITORING ANALYSES



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DEPARTMENT  
OF MICROBIOLOGY

## Keeping a close eye on influenza

Virology and serology (VIRO) and epidemiology and microbial genomics (EPIGEM) are two units of the microbiology department. For several years, they have played an essential role in the sentinel surveillance of influenza.

Every year, from October to April in the northern hemisphere and from April to October in the southern hemisphere, flu outbreaks affect millions of people worldwide. Although seasonal influenza generally remains mild, it is still responsible for millions of severe cases and hundreds of thousands of annual deaths. According to the European Centre for Disease Prevention and Control (ECDC), between 291,000 and 646,000 people worldwide die from a seasonal influenza-related respiratory illness every year.

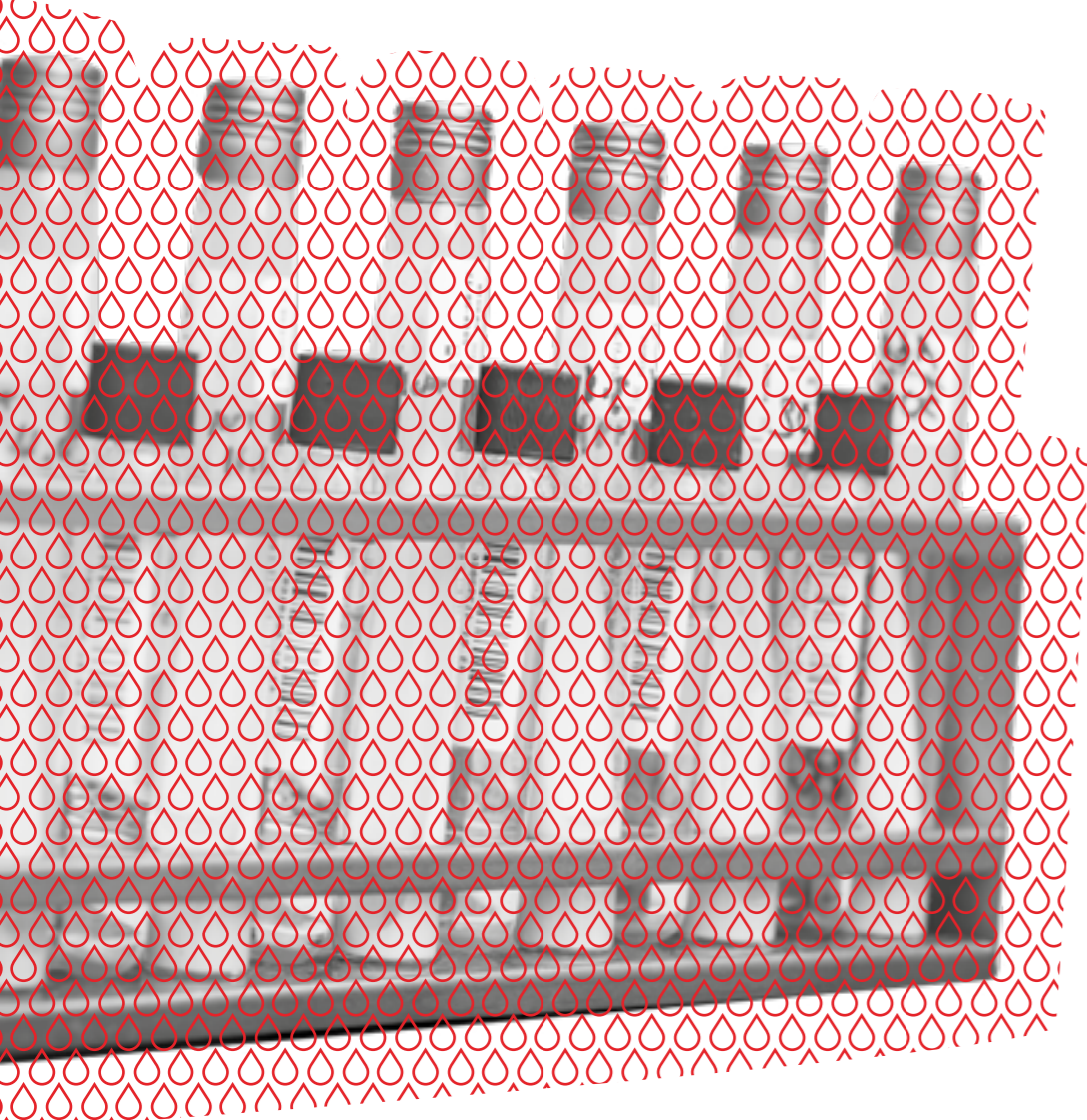
Influenza, commonly known as flu, is an infectious disease caused by viruses of the Orthomyxoviridae family. This family of viruses mainly attacks the respiratory tract (nose, throat and bronchi). The symptoms appear 1 to 4 days after infection and are characterised by a sudden onset of high fever, muscle pains, headaches, generally feeling unwell, dry cough, sore throat and runny nose. Although most affected people recover in one or two weeks without medical treatment, flu can have a severe impact in vulnerable populations such as young children, the elderly and people suffering from chronic diseases (lung, heart and kidney problems, cancer, immunosuppression, etc.). For these risk groups, vaccination against influenza is recommended.

*"WE ARE THE ONLY LABORATORY IN THE COUNTRY TO DIAGNOSE AND HANDLE HIGHLY PATHOGENIC INFLUENZA VIRUSES."*

**DSc Guillaume Fournier**

Deputy head of the virology and serology service





## A WIDE VARIETY OF CHANGING VIRUSES

“To tackle seasonal outbreaks, sophisticated surveillance has been established at both national and international levels”, explained DSc Guillaume Fournier, deputy head of the virology and serology unit. “But the task is not easy. Since the common cold and influenza share symptoms, it can be difficult or even impossible to tell the difference between them based on the clinical presentation alone. Often people don’t realise that they have the flu. In 80% of the cases, influenza infection goes unnoticed or only appears to be a mild cold.”

“Also, not a single but several viruses cause influenza. There are three types of influenza virus in humans: A, B and C. Types A<sup>1</sup> and B are frequently at the origin of outbreaks and type A can sometimes cause a pandemic. This is made possible by permanent genetic changes through two mechanisms. The first mechanism is called antigenic drift. Small changes in the genes of the virus happen continually over time as the virus replicates.

These small genetic changes usually produce viruses that are closely related to one another, but can accumulate over time and result in antigenically different viruses. When this happens, the body’s immune system may not recognise those viruses. The other type of change is called antigenic shift and is an abrupt, major change in the influenza A virus, resulting in new proteins at the surface of the virus. This new virus may be so different to such an extent, that most people do not have any immunity and thus the virus quickly spreads, causing a pandemic.”

The continuous genetic modifications of influenza viruses make it necessary to adjust the composition of the the influenza vaccine every year. For this, the worldwide network of the World Health Organization (WHO) collects and analyses virology and epidemiological influenza surveillance data from around the world. The regular exchange of these data in-between countries allows WHO in the selection of influenza strains chosen for subsequent vaccine production.

<sup>1</sup> Type A viruses are divided into subtypes based on the nature of their surface proteins: hemagglutinin (H1 to H18) and neuraminidase (N1 to N11).

## THE PRINCIPAL ROLE OF THE DEPARTMENT IN THE SENTINEL SURVEILLANCE

In Luxembourg, the department of microbiology, the *Direction de la Santé* and a network of general practitioners and paediatricians throughout the country work together every year, from October to April, to ensure sentinel surveillance of influenza. “The doctors of the network report to us once a week the proportion of patients presenting an acute respiratory infection (ARI) or an influenza syndrome (ILI) during one day in the week”, said DSc Guillaume Fournier. “In parallel, they take nose/throat samples from ILI patients and send them to our department. We analyse them by using polymerase chain reaction (PCR) and sequencing methods to detect the presence of influenza virus and to characterise the type and strain of the virus. Once a week, we update the influenza activity and inform the doctors, the *ministère de la Santé* and the general public via our newsletter and the influenza surveillance section of the LNS website. At the same time, we transmit our statistics and our PCR results to ECDC.”

“At the end of the flu season, we dispatch all our data on strains of influenza viruses that have circulated in Luxembourg to the European and world authorities (ECDC and WHO) in order to allow them to perform a global epidemiological monitoring

and to perform appropriate strains to include in the vaccine for the next epidemic season. Seasonal flu may change from one year to another. For example, the season 2017-2018 was particularly intense. We received two to three times more samples than the previous year: 2,000 with 54% positive versus 600 with 36% positive. Circulating viruses were also very diversified: 27% B, 24% A H1N1 and 3% A H3N2.”

## NATIONAL REFERENCE LABORATORY FOR FLU AND OTHER INFECTIOUS DISEASES

Sentinel surveillance is only a part of the LNS missions as a national reference laboratory for influenza. “We also bring our expertise to hospitals and other laboratories and help them in case of epidemics or discovery of an unexpected subtype”, added DSc Guillaume Fournier. “We are the only diagnostic laboratory in the country to have an operational biosafety level 3 (BSL-3) facility dedicated to influenza surveillance. It means that our working environment allows us to diagnose and handle highly pathogenic influenza viruses. And since the Law of 1 August 2018 on the compulsory declaration of certain diseases in the framework of the protection of public health, the role of the microbiological department in the surveillance of certain infectious diseases will certainly increase.”



Virology and serology team

## Bacteriology, mycology, antibiotic resistance and hospital hygiene

### ACTIVITIES

- 2 successful challenges:
  - > Installation of the Antibiotic Resistance Platform, as part of the 2018-2022 National Antibiotic Plan, to centralise antibiotic resistance data for the entire country.
  - > ISO 15189 accreditation of the whole "Mycobacteria" sector, from direct examination to the antibiogram via the PCR and the cultures, making the LNS 'Mycobacteria' sector the first accredited P3 laboratory of Luxembourg.
- 4 rising business sectors:
  - > The "Mycobacteria" sector where the MTB/MDR PCR, implemented during the year, now allows the detection of multi-resistant tuberculosis directly from the clinical sample.
  - > The "Mycology" sector, a cutting-edge diagnostic sector, in particular thanks to its 2 in-house PCRs (PCR Dermatophytes and PCR Trichophyton rubrum on clinical sampling), and its ability to sequence fungal pathogens detected in culture (dermatophytes, filamentous fungi or yeasts).
  - > The "Genital Samples" sector, which offers a wide range of ISO 15189 accredited analyses, both in terms of PCR (C. trachomatis, N. gonorrhoeae, T. vaginalis and M. genitalium) and specific cultures (N. gonorrhoeae, urogenital mycoplasma, yeasts).
  - > The "Strains: Identification, Antibiogram and Molecular Typing" sector, which has seen an explosion in the number of requests for sequencing analysis of the entire genome (WGS analysis: +220% in one year), mainly for the comparison of multi-resistant hospital strains: MRSA, ERV or Enterobacteriaceae producing carbapenemases.
- The service supervised 2 trainees and welcomed its infectious disease specialists and microbiologists from the CHL, as well as family planning doctors from across the country.
- 3 posters were produced, including one in collaboration with the LMVE (veterinary medicine laboratory) and presented at the RICAI congress in Paris in December 2018.

**34,990**

ANALYSES

## Virology and serology

### ACTIVITIES

- As the national reference centre for influenza, the virology unit recorded a higher level of influenza activity during the winter 2017-2018. The epidemic was marked by the predominance of types B (Yamagata lineage) and A (H1N1v). In particular, the laboratory absorbed part of the activity of hospitals following the failure of certain commercial rapid tests.
- Participation to the starting Metagenomics project addressing meningoencephalitis etiology. The aim is to evaluate, at the request of CHL clinicians, the relevance of next generation sequencing approach in order to identify possible infectious agents in idiopathic meningoencephalitis cases.
- Active collaboration with the Luxembourg Institute of Science and Technology (LIST) to develop a common approach to sequence clinical and environmental enteroviruses.
- Implementation of BSL-3 Laboratory procedures for operational and effective responses to a series of biological threats.
- Participation in the 3rd meeting of the Emerging Viral Diseases Laboratory Network (EVD-LabNet) to develop diagnostic tools for vector-borne diseases.

**27,957**

SEROLOGY  
ANALYSES

**15,123**

PCR ANALYSES  
IN VIROLOGY

**86**

CELL CULTURES

## Epidemiology and microbial genomics

### ACTIVITIES

- Successful participation in European foodborne pathogen surveillance based on whole genome sequencing: compared national data to 40 international outbreaks strains. 1400 isolates sequenced by whole genome analysis.
- New research projects including CampyLOmic (One Health Genomics of Campylobacter) involving 5 partners, a doctoral training unit MICROH (Microbiomes in One health) funded by FNR; authorisation to supervise PhD students obtained by Catherine Ragimbeau and Joël Mossong, PhD; recruitment of PhD student and a post-doc.
- Start of international development project CARES in Senegal and Guinea-Bissau funded by the *ministère de la Coopération* on HPV in collaboration with LIH and CHL.
- Implementation of a collaborative research project with CHL physicians to use metagenomics for diagnosing meningo-encephalitis funded by the Personalised Medicine Consortium.
- Successful first participation in the food metagenomics ring trial by the EU funded project COMPARE.
- 6 publications in peer-reviewed journals; 5 presentations at international conferences; 1 prize award for best PhD presentation by Dr Ardashes Latsuzbaia.

**9,742**

MOLECULAR  
BIOLOGY ANALYSES

**1,400**

WHOLE GENOME  
ANALYSES



# 2018

## NATIONAL CENTER OF GENETICS

## The National Center of Genetics has become a reality

2018 was a pivotal year for the department of genetics. Established in 2016 and based on a concept for a national genetic center that was approved as part of the *Plan National Cancer* (2014-2018), the department officially became the National Center of Genetics (NCG) this year.

*"THE PURPOSE OF THE NCG IS TO COVER ALL ASPECTS OF HUMAN GENETICS NEEDED IN LUXEMBOURG, IN PARTICULAR ENSURING COMPREHENSIVE MEDICAL CARE AND PROVIDING GENETIC TESTING FOR THE WHOLE POPULATION."*

**Dr Barbara Klink**  
Head of National Center of Genetics



"The purpose of the NCG is to cover all aspects of human genetics needed in Luxembourg, in particular ensuring comprehensive medical care and providing genetic testing for the whole population", said Dr Barbara Klink, a specialist in human genetics appointed in May 2018 as head of the new center. "This includes, among others, genetic counselling and management of patients in multidisciplinary settings, a broad spectrum of genetic diagnostics for hereditary diseases, genetic characterisation of cancer for diagnostic and therapeutic indications. Furthermore, it needs constant development and subsequent implementation of novel genetic tests and methods to carry out up-to-date diagnostics, patient centred health research and translational research for genetic diseases. The NCG also offers expert advice to different stakeholders (for example clinicians, representatives from the *ministère de la Santé*, participants in the *Plan National Cancer*). We actively take part in the *Plan National Maladies Rares* that started in 2018, both within the board but also in specific working groups. In addition, since implementation of the new hospital law from 8 March 2018, all the genetic diagnostic tests performed in Luxembourg is managed by the NCG."

#### AMBITIOUS GOALS AND SIGNIFICANT ACHIEVEMENTS

To achieve these ambitious goals, the centre had to undergo profound and rapid development. "And we are only at the beginning", pointed out Dr Barbara Klink. "Many employees, including me, were hired in 2018 and the recruitment process is not finished. Key positions are still vacant and finding genetic specialists is a challenge. Genetics is a relatively new, rapidly developing and complex discipline. Around 80% of the 8,000 rare diseases identified are of genetic origin. Thanks to new techniques, such as Next Generation Sequencing (NGS), we discover more and more disease-related genes responsible for rare hereditary diseases, and this number is constantly growing."

Despite this challenging situation, the center accomplished many significant achievements during this short period. "In order to cover the spectrum of necessary genetic methods, genetic diagnostics are performed within three units: a cytogenetic unit, a molecular genetic unit and a haematology unit", explained Dr Barbara Klink. "In all the units, there was considerable growth in the diagnostic activity in the last two years. Taken together, 7,897 genetic tests were conducted in 2018 compared to approximately 4,200 tests in 2016. We expect that the number of tests will further increase in 2019 (indeed more than 11,000 tests are projected). An important step in 2018 was the implementation of LuxGen. This common sequencing platform between the Luxembourg Institute of Health (LIH) and the LNS is located at the NCG and allows us to provide state-of-the-art Next Generation Sequencing (NGS) based genetic diagnostics. New diagnostic tests were also introduced, such as genetic testing for cystic fibrosis in January 2018 and genetic diagnostic of hereditary tumour diseases using a multi-gene sequencing panel in April 2018. A non-invasive prenatal testing (NIPT) platform for trisomy 13, 18 and 21 (Down syndrome) was purchased in December 2018 and we expect to start in the third quarter of 2019 with routine diagnostics. We are assuming that approximately 5,000 to 6,000 NIPTs will be requested per year."

"We have also made an important step to push forward the personalised cancer medicine in Luxembourg", added Dr Barbara Klink. "We are currently testing different larger cancer panels to allow for a more comprehensive characterisation of cancers in the future. These tests currently do not form part in routine diagnostics and are restricted to cases in which standard treatment has failed. They help to identify alternative treatment options. They are performed in close collaboration with the National Center of Pathology (NCP) at the LNS and the Institut National du Cancer (INC) in Luxembourg. Furthermore, as of December 2018, the NCG and NCP participate at the newly implemented molecular tumour board organised by the *Institut National du Cancer*."



## A SHARP INCREASE IN GENETIC CONSULTATIONS

Genetic counselling is another central part of the activities of the NCG. It aims to provide information to patients and their families about genetic testing and their genetic disease: its nature, mode of inheritance, risk for other family members, genetic testing to establish or confirm the diagnosis.

"We are working in close partnership with the hospitals and doctors from different disciplines", continued Dr Barbara Klink. "When they suspect a genetic disease, they either send us a sample for genetic testing or refer the patients to us for genetic counselling, depending on the type and complexity of disease. We also discuss patients in multidisciplinary meetings. In any case, if there is a positive (pathological) test result, this should be communicated and explained to the patient in the framework of genetic counselling. Before we can perform a genetic test, we need an informed consent of the patients. This is very important, since a genetic test result can have many implications, not only for the individual themselves, but also for their families.

We perform genetic consultations in the context of constitutional genetic disorders such as intellectual disability or genetic predisposition of cancers, but also preconception and prenatal genetic counselling."

"The number of genetic consultations increased considerably in 2018. We saw more than 780 families - 918 patients - for genetic counselling, compared to 480 families in 2017. Since October 2018, we offer genetic counselling in French, German and English. Furthermore, we participate in the weekly prenatal multidisciplinary meeting at the CHL. We aim to increase our counselling activity - estimated are 2000 families per year in the future - and our interdisciplinary work in line with our capacities."

"The NCG is an exciting project", concluded Dr Barbara Klink. "We establish the entire spectrum of human genetics in Luxembourg: diagnostics, clinical service, translational research, and academic activities."



## National Center of Genetics

### MOLECULAR GENETICS

**4,291**

CONSTITUTIONAL  
GENETIC ANALYSES

**1,179**

SOMATIC GENETIC  
ANALYSES

CYTOGENETICS

ONCO-HAEMATO-  
LOGICAL GENETICS

**1,253**

CYTOGENETIC ANALYSES

**1,174**

ONCO-HAEMATOLOGICAL  
ANALYSES

HAEMOGLOBINO-  
PATHIES

**2,537**

HAEMOGLOBIN  
SEPARATION AND  
QUANTIFICATION ASSAYS

GENETIC  
COUNSELLING

**918**

PATIENTS AND FAMILIES  
SEEN AT THE LNS OR  
EXTERNAL HOSPITALS FOR  
GENETIC CONSULTATIONS



## Cystic fibrosis screening available to all newborns

The neonatal screening and metabolic diseases unit of the department of medical biology aims to identify babies born with rare diseases, often of genetic origin. The aim is to diagnose these diseases as quickly as possible and apply effective treatment during the first days of life in order to prevent severe deficiencies or even death. So far, the unit has been detecting the following four diseases by using dried whole blood spots: phenylketonuria, congenital hypothyroidism, congenital adrenal hyperplasia, and medium-chain acyl-coenzyme A dehydrogenase (MCAD) deficiency. On 2 January 2018, it launched a new pilot project under the auspices of the *Direction de la Santé*: the cystic fibrosis screening for all babies born in Luxembourg.

*"RESEARCH HAS SHOWN THAT CHILDREN WHO RECEIVE CYSTIC FIBROSIS CARE EARLY IN THEIR LIFE HAVE BETTER HEALTH OUTCOMES THAN THOSE DIAGNOSED LATER."*

**Dr pharm. DSc Patricia Borde**  
Head of the department





## THE IMPORTANCE OF AN EARLY DIAGNOSIS

Cystic fibrosis is an inherited and incurable disease that causes the body to produce excess mucus that is abnormally thick and sticky; symptoms are usually nutritional disorders and frequent bronchopulmonary infections. Research has shown that children who receive cystic fibrosis care early in life have better health outcomes than those who are diagnosed later. Early diagnosis and treatment improves growth, helps keep lung healthy, reduces hospital stays and adds years to life.

“Newborn screening for cystic fibrosis is slightly different from other programs in the sense that it is carried out in collaboration with the National Center of Genetics and the Luxembourg Centre for Cystic Fibrosis and Related Diseases”, says Dr pharm. DSc Patricia Borde, head of the department. “Screening is done on the same dried blood sample, the Guthrie card, like that used for other diseases, at the same age of the child - i.e., 72 hours of life - and is based on a two-step technique.”

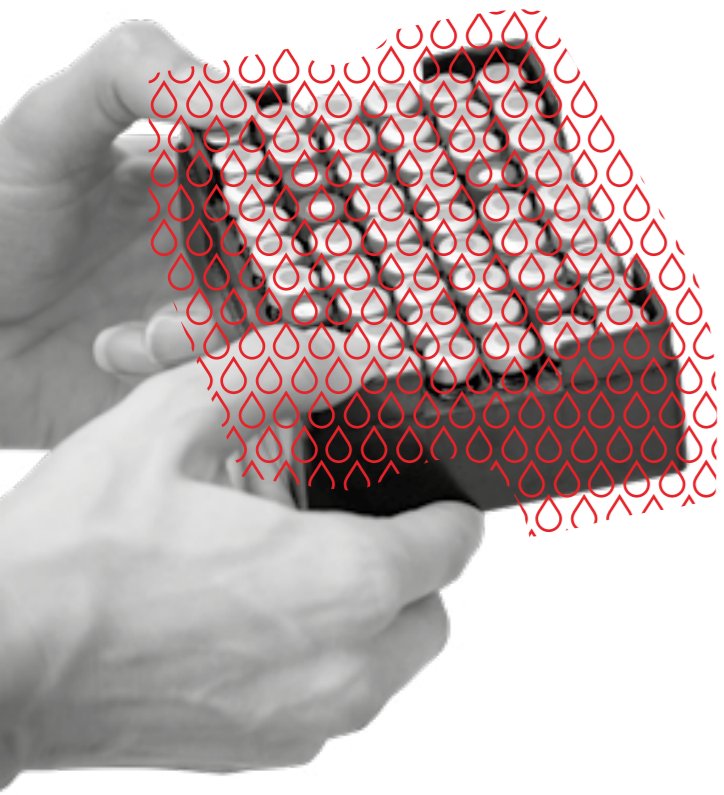
The first step is the measurement of a biomarker, immunoreactive trypsin (IRT), on the blood sample. If the concentration of IRT is out of the normal range and if written parental consent is obtained, the Guthrie card is transferred to the National Centre of Genetics for DNA testing. In the absence of written permission, the parents are contacted by the maternity ward and informed of the need to continue the examinations by a second IRT measurement on a second Guthrie card. The genetic test does not cover all the possible mutations of the so called cystic fibrosis transmembrane conductance regulator (CFTR) gene – there are more than 2,000 – but the 50 most frequent are included, which is high number compared to the neighbouring countries<sup>1</sup>.

## THE RELEVANCE OF THE SWEAT CHLORIDE TEST

Different situations are possible subsequent to the genetic analyses. If two mutations are identified, the baby must be seen in a specialised centre, the Luxembourg Centre for Cystic Fibrosis and Related Diseases (*Centre Luxembourgeois de Mucoviscidose et des Maladies apparentées* or CLMMA) at the *Centre Hospitalier de Luxembourg* (CHL), to rule out or confirm the diagnosis by a sweat chloride test. This test measures the amount of chloride in the child’s sweat. Chloride is part of the body’s electrolyte balance and combines with sodium to form the salt found in sweat. A colourless and odourless chemical that causes sweating (pilocarpine) is applied to a small area of skin (usually on the arm or leg). An electrode is then placed over the spot to induce sweating. The procedure does not cause any pain at all, only a feeling of warmth in the area. The sweat is collected on a piece of filter paper or gauze or in a plastic coil and sent to the hospital laboratory for evaluation. Children with cystic fibrosis have an elevated level of chloride in their sweat.

If only a single mutation is detected, the child may be a healthy carrier of the disease (as is one of the parents), which is most likely, or the child may have cystic fibrosis. A sweat chloride test at the CHL is also needed in this case. If no mutation is detected, an IRT rate-check is performed on Day 21. If the rate is still above the average, the child must be seen at the CLMMA where investigations will be carried out. In most of these cases, further investigations may make it possible to confirm the diagnosis.

<sup>1</sup> In France, the DNA testing detects the 30 most frequent mutations.



### SEVERAL CLINICAL FORMS OF THE DISEASE

“For some children, it may be difficult to establish a firm diagnosis”, specified Dr pharm. DSc Patricia Borde. “The baby may have an intermediate sweat test and does not carry mutations or sometimes one or two particular mutations. The clinical expression of the disease can be highly variable. There is not one but several clinical forms of the disease.”

One year after the launching of the project, Dr pharm. DSc Patricia Borde has come to a positive conclusion. “Of the 7,245 Guthrie cards we received in 2018, we have detected three in which babies are found to have a serious form of cystic fibrosis. That tends to prove that our screening is useful and can make the lives of children with this disease healthier. We are working now to improve the consent form to be signed by the parents. They are sometimes very concerned when they learn that genetic tests may be required for their child. It is important to mention that a high IRT level is not specific to cystic fibrosis. A large number of newborns have hypertrypsinemia without having cystic fibrosis. In addition, genetic testing is restricted to the CFTR gene and not on all the genes of the child. A brochure, written in four languages (English, French, German and Portuguese) will be published in the first quarter of 2019 by the *ministère de la Santé* to better explain to parents the usefulness and need of this test.”



## Medical biology

### ACTIVITIES

- Launch of specialised allergy tests in July. These tests make it possible to diagnose and identify the mechanisms at the origin of drug allergies or against hymenopteran venoms, and to monitor the effectiveness of desensitisation protocols. They are prescribed by allergists and accompanied by an evocative clinical history.
- Acquisition of a brand-new mass spectrometer to develop toxicological analyses and accelerate the turn-around time of metabolic analyses, amino acids in particular.

**36,225**

NEONATAL SCREENING ANALYSES

**1,400**

ANALYSES OF RARE METABOLIC DISEASES

**11,144**

PRENATAL SCREENING ANALYSES

**25,744**

CLINICAL TOXICOLOGY ANALYSES

**27,127**

HORMONAL ASSAYS

**101,640**

TOTAL NUMBER OF ANALYSES



0218

DEPARTMENT OF  
ADMINISTRATION, FINANCE  
AND SUPPORT SERVICES

## Towards full digitalisation

The information technology (IT) service is responsible for setting, administering and developing IT systems and networks for the professional activities of LNS. In 2018, the service was involved in two essential projects aiming to digitalise data transmission: eHospital and eDoctor.

*"THE DIGITALISATION OF THE DATA TRANSMISSION HAS HAD A POSITIVE IMPACT ON THE IMAGE OF LNS AND STRENGTHENED THE TRUST OF OUR STAKEHOLDERS."*

**Thibaut Lenfant**  
IT manager





## MORE TRANSPARENCY AND TRACKABILITY

“As a national reference laboratory, we receive each year hundreds of thousands requests for sample medical analysis from our different stakeholders: doctors, hospitals and private laboratories”, commented Thibaut Lenfant, head of the service. “According to our estimations, we receive 232,280 requests per year, which represent 1,106,255 paper mailings of reports, and this number will increase over time. Thanks to the digitalisation of the LNS transmission data, we can save paper on reports, but that is not the only advantage! The global traceability process and data tracking will be improved. In the future, all the samples will be univocally identified and localised before the reception process inside LNS. Every data creation, modification, deletion and transfer will be stored and tracked, which will give more transparency between all the actors: LNS, prescribers and partner organisations. Data digitalisation will ensure stable and standardised data throughout the process with all the stakeholders and will reduce transmission times.”

“More specifically, we want to create a bidirectional model that will appear as follows. LNS will offer its analysis catalogue online, which will allow partners to place their e-orders and send them electronically to LNS. By doing so, they will generate unique IDs which will make the link between each e-prescription and each sample and will guarantee sample tracking between the different stakeholders. Finally, the results will be sent electronically. The whole process – from prescriptions to results - will be fully digital.”

## THE FIRST STEPS: eHOSPITAL AND eDOCTOR

Since 2017, the IT unit has been initiating the first steps of LNS digitalisation. “We launched this year the test and pilot phases of our eHospital project”, detailed Thibaut Lenfant. “The ultimate purpose is to enable the exchange of structured data - names and codes of the doctor and of the patient, date and time of the sampling, date and time of the analysis, etc. - with the private laboratories and the four hospitals of the country (via the HL7 protocol<sup>1</sup>) and the *ministère de la Santé* (via the XML language). In 2018, we went to the production phase to deliver the reports directly to the patient files of two hospitals. At the moment, the exchange is only unidirectional. Our next challenge will be to make it bidirectional. We will do this at first with one hospital by implementing an electronic order entry system. This electronic database will aim to ensure single identity management for each patient inside LNS, which represents the missing link to simple, reliable and quality information for effective exchanges with the LNS partners.”

In November 2018, the service initiated the eDoctor project. “The objective is to connect the 140 doctors with whom we have many activities – they send more than 100 prescriptions per year to LNS”, explained Thibaut Lenfant. “The pilot phase during which we deliver the reports to 20 doctors both electronically (via the exchange data solution Regibox) and paper-based will end after the validation process in 2019. After this phase, paper-based transmission will be removed at the request of the recipient.”

According to Thibaut Lenfant, electronic data transmission is on the way to becoming the routine in coming years. “We are expecting a growing number of digitally delivered results. In 2019, around a fifth of the reports - 225,000 out of a total of 1,100,000 – will be digital. In addition, this digitalisation has had a positive impact on the image of LNS and strengthened the trust of our stakeholders. For example, we found that the doctors involved in the pilot phase of the eDoctor project sent us many more diagnostic test requests than in the past!”



<sup>1</sup>HL7 is a set of international standards used by healthcare providers transferring clinical and administrative data between software applications.

## Finance

### ACTIVITIES

- 2018 represents a significant change in the accounting and budgetary practices, as a result of the new financial structuring of the LNS due to the entry into force of the hospital law on 1 April. This law fundamentally alters the funding flows: CNS funds pathology and genetics activities according to the same principle as hospitals, while other scientific departments remain funded by the *ministère de la Santé*, the *ministère de la Justice* and the invoicing of analyses.
- This situation introduces a duality into accounting and budgetary practices. The CNS's accounting rules differ significantly from the Luxembourg accounting standards applicable to a commercial company and used at LNS. This duality also applies to the budget year which must be produced for the entire LNS activity as well as for the CNS. Moreover, this also applies to the budget exercise, which is duplicated since we have to produce a budget for the entire activity of the LNS and also for the CNS. Hospital law not only implies a significant increase in activity for the controlling unit, but also for the billing unit. Indeed, although they existed before April 1, 2018, pathology and genetics activities were not invoiced up to that date.

## Infrastructures and logistics

### ACTIVITIES

- Planning and implementation of the relocation measures of the department of medical biology laboratories following their move to the 5th floor (completion: May 2018).
- Construction of a new storage facility with electric mobile racks for the storage of paraffin blocks/slides of the National Center of Pathology (completion: May 2018).
- Preparation of tender documents for the public tender for the project "MBC Laboratory".
- Development of a maintenance database / GMAO (Gestion de Maintenance assistée par Ordinateur) for the planning of regular and preventive maintenance.
- Installation of modern media technology in the conference room (completion: July 2018).

### ENERGY CONSUMPTION

**5,303** **584,944**

MWh ELECTRICITY

m<sup>3</sup> GAS

**2,240** **2,590**

MWh COLD

MWh HEAT

### CENTRAL WAREHOUSE

**12,257** **910**

STOCK MOVEMENTS  
(STOCK RECEIPT AND  
STOCK ISSUE)

DIFFERENT ARTICLES ARE  
STORED IN THE CENTRAL  
WAREHOUSE

## IT

### ACTIVITIES

- Upgrade of our transverse analysis management system, Glims, to be ready for digitalisation.
- Pilot phase of the eDoctor project with 20 doctors to deliver them analysis reports digitally.
- Production phase of the eHospital project to deliver the reports directly to the patient files of 2 hospitals.
- Telepathology project in production in 4 hospitals.
- New backup system ready to manage the exponential growth of data managed inside LNS.

**20**

DOCTORS CONNECTED  
VIA eDOCTORS

**40,000**

REPORTS SENT ELECTRO-  
NICALLY VIA eHOSPITAL

**> 150**

VIRTUAL SERVERS

**3,000**

HELPDESK REQUESTS

**550**

MANAGED COMPUTERS

**150 TB**

OF DATA

## Human resources

### ACTIVITIES

- Recruitment in support of significant growth and organisational development.
  - > More than 50 new recruits in 2018 (approx. 50 new recruits in 2017) + 50 students and interns.
- Enhanced communication and strong reputation as trusted HR business partners.
  - > Active support to managers and employees, particularly in solving complex staffing and organisational issues.
  - > Performance management review and workgroup.
- Proactively catering to public employees.
  - > Successful implementation of CET (*Compte Epargne Temps*) for public employees.
- Creating a robust, structured and modern HR service model.
  - > Streamlining HR administrative processes, recruitment module through ERP.

**265.5**

FULL-TIME  
EQUIVALENTS

**18**

NEW POSITIONS  
(excluding replacements)

**50**

NEW RECRUITS  
(18 fixed-term and  
32 permanent contracts)

**42.7**

AVERAGE AGE OF STAFF

**64.4%**

WOMEN

**35.6%**

MEN

**15**

NATIONALITIES

FINANCES

# 03

## Assets

	2018	2017
<b>Fixed assets</b>		
<b>Intangible fixed assets</b>		
Concessions, patents, licenses, trademarks and similar rights	462 625,25	362 448,11
Advances paid and intangible assets in progress	-	8 500,00
	<b>462 625,25</b>	<b>370 948,11</b>
<b>Tangible fixed assets</b>		
Land and buildings	79 482 896,14	82 694 380,74
Technical installations and machines	3 873 820,18	3 514 421,81
Other installations, tools and furniture	822 606,52	686 489,84
Advances paid and tangible fixed assets in progress	5 040,24	84 315,62
<b>TOTAL FIXED ASSETS</b>	<b>84 184 363,08</b>	<b>86 979 608,01</b>
<b>Current assets</b>		
<b>Stocks</b>		
Raw materials and consumables	218 803,42	142 672,40
<b>Debtors</b>		
Trade debtors		
- Becoming due and payable within one year	<b>9 404 922,82</b>	<b>2 055 081,35</b>
<b>Other debtors</b>		
- Becoming due and payable within one year	13 938 075,81	13 384 066,00
- Becoming due and payable after more than one year	288 577,29	293 978,89
Cash at bank and in cash	5 097 832,40	8 522 321,05
<b>TOTAL CURRENT ASSETS</b>	<b>28 948 211,74</b>	<b>24 398 119,69</b>
<b>Deferred cost</b>		
	178 521,19	220 134,53
<b>TOTAL ASSETS</b>	<b>113 773 721,26</b>	<b>111 968 810,34</b>

## Liabilities

	2018	2017
<b>Equity</b>		
Retained earnings	5 195 323,84	7 701 925,61
Profit or loss of the year	3 226 649,76	(2 506 601,77)
Capital investment subsidies	82 600 882,48	87 350 556,12
<b>TOTAL EQUITY</b>	<b>91 022 856,08</b>	<b>92 545 879,96</b>
<b>Provisions</b>		
<b>Other provisions</b>	<b>4 516 836,54</b>	<b>3 842 807,06</b>
<b>Debts</b>		
<b>Trade debts</b>		
- Becoming due and payable within one year	2 885 877,33	1 243 835,58
<b>Other debts</b>		
Tax debts	222 468,68	-
Social security debts	404 241,21	403 512,61
Other debts: becoming due and payable within one year	13 938 407,79	13 394 474,77
<b>TOTAL DEBTS</b>	<b>17 450 995,01</b>	<b>15 041 822,96</b>
<b>Deferred income</b>		
	783 033,63	538 300,36
<b>TOTAL LIABILITIES AND EQUITY</b>	<b>113 773 721,26</b>	<b>111 968 810,34</b>

## Profit and loss account

	2018	2017
<b>Net turnover</b>	21 057 348,86	6 353 192,74
<b>Other operating income</b>	30 011 617,82	37 062 611,64
<b>Use of merchandise, raw materials and consumable materials</b>		
Raw materials and consumable materials	(6 797 082,04)	(5 010 774,73)
Other external expenses	(19 928 447,63)	(18 679 107,85)
<b>Staff costs</b>		
Wages and salaries	(10 825 027,26)	(8 401 742,27)
Social security contributions covering pensions	(767 870,10)	(571 991,79)
Other social expenses	(508 890,23)	(421 433,30)
<b>Value adjustment</b>		
On intangible and tangible fixed assets	(6 441 424,66)	(9 458 509,20)
<b>Other operating expenses</b>	(2 575 316,06)	(3 383 654,72)
<b>Other interests and other financial income</b>		
Other interests and financial income	2 049,73	4 873,11
<b>Interests and other financial expenses</b>		
Other interests and financial expenses	(308,67)	(65,40)
<b>NET RESULT FOR THE YEAR</b>	<b>3 226 649,76</b>	<b>(2 506 601,77)</b>



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04

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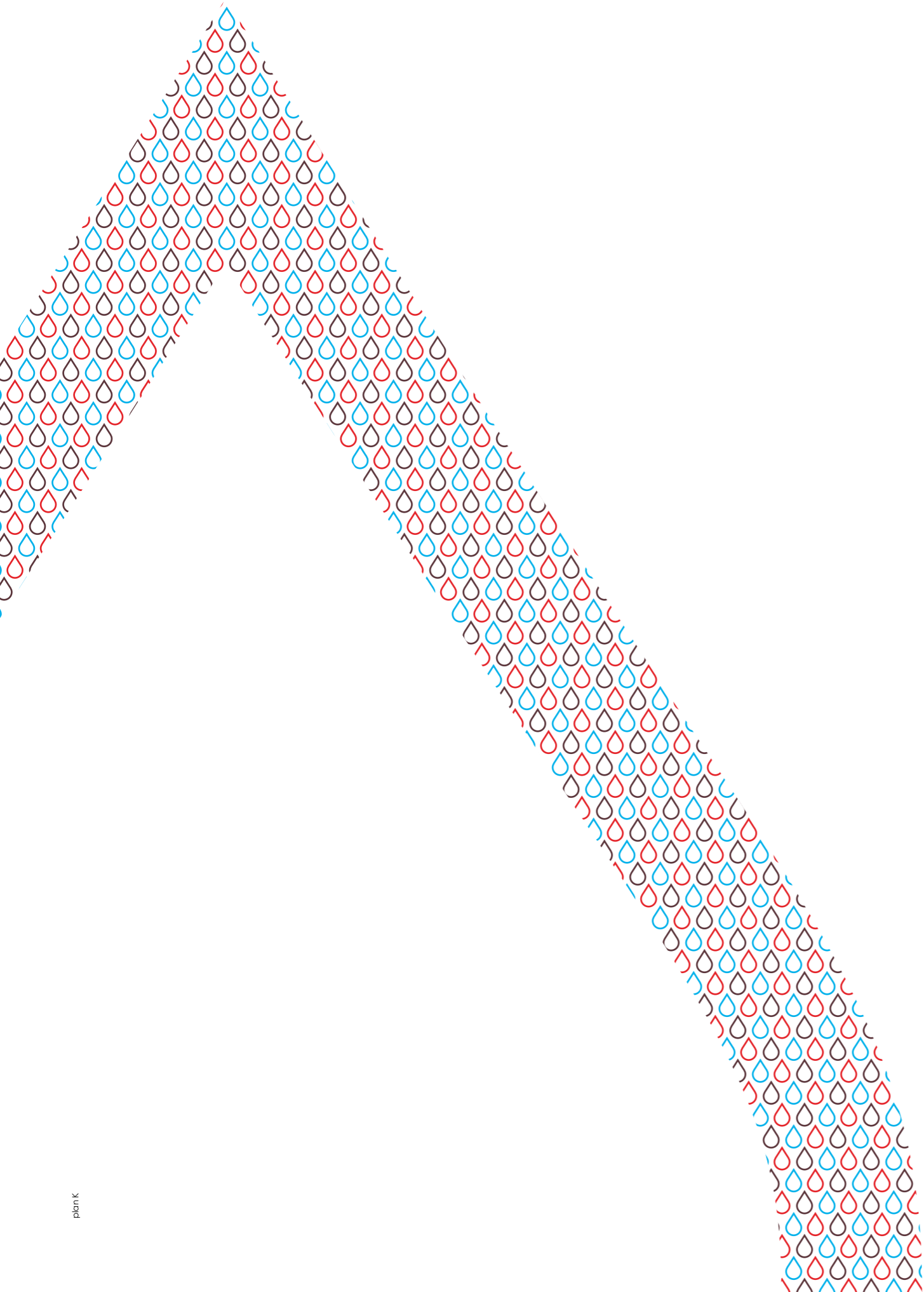
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