ToxAlim - Toxicologie alimentaire

Rapport Hcéres

HCERES

High Council for the Evaluation of Research and Higher Education

Research units

HCERES report on research unit:

Research centre in Food Toxicology

TOXALIM

under the supervision of the following institutions and research bodies:

Institut National de la Recherche Agronomique - INRA

Institut National Polytechnique de Toulouse - INP Toulouse

Université Toulouse 3 - Paul Sabatier - UPS

Evaluation Campaign 2014-2015 (Group A)

HCERES

High Council for the Evaluation of Research and Higher Education

Research units

In the name of HCERES,[1]

Didier HOUSSIN, president

In the name of the experts committee,[2]

Eugenia DOGLIOTTI, chairwoman of the committee

Under the decree No.2014-1365 dated 14 november 2014,

[1] The president of HCERES "countersigns the evaluation reports set up by the experts committees and signed by their chairman." (Article 8, paragraph 5)

[2] The evaluation reports "are signed by the chairman of the expert committee". (Article 11, paragraph 2)

Evaluation report

This report is the result of the evaluation by the experts committee, the composition of which is specified below.

The assessments contained herein are the expression of an independent and collegial deliberation of the committee.

Unit name:	Research centre in Food Toxicology
Unit acronym:	TOXALIM
Label requested:	UMR
Present no.:	1331
Name of Director (2014-2015):	Mr Bernard SALLES
Name of Project Leader (2016-2020):	Mr Bernard SALLES

Expert committee members

Chair: Ms Eugenia DOGLIOTTI, Istituto Superiore di Sanità, Rome, Italy

Experts: Ms Giovanna CADERNI, University of Florence, Italy

Mr Francois CASAS, INRA, Montpellier, France (representative of CSS)

Mr Xavier COUMOUL, Université René Descartes, Paris

Mr Paul A. FOWLER, University of Aberdeen, Scotland

Mr Theo NIEWOLD, University of Leuven, Belgium

Scientific delegate representing the HCERES:

Mr Jean-Francois HOCQUETTE

Representatives of the unit's supervising institutions and bodies:

Mr Jean DALLONGEVILLE, INRA, AlimH

Mr Claude MARANGES (Doctoral school UPS - Sciences écologiques, vétérinaires, agronomiques et bioingenieries ED n°458)

Mr Alain MILON, École Nationale Vétérinaire de Toulouse - ENVT

Mr Thierry PINEAU, INRA, SA

Mr Michel ROUX, École d'Ingénieurs de Purpan - EI-Purpan

Mr Alexis VALENTIN, Université Toulouse 3 - UPS

Mr Philippe VALET (Doctoral school UPS - Biologie, santé, biotechnologies ED n°151)

1 • Introduction

History and geographical location of the unit

TOXALIM is a joint research unit (UMR) created in 2011 by merging four research units present in Toulouse, from INRA (UR 66 "Pharmacology and Toxicology"), INRA/ENVT (UMR 1089 "Xenobiotics" and UMR 181 "Physiopathology and Experimental Toxicology") and INRA/EIP (UMR 1054 "Neuro-Gastroenterology and Nutrition"). The aim was to create the largest unit in France in the area of food toxicology. The director, Mr Bernard SALLES, came with part of his team from CNRS/University (UMR 5089). TOXALIM is under the supervision of INRA divisions ALIMH (Human Nutrition) and SA (Animal Health). The geographic location of TOXALIM results in a degree of isolation with respect to the location of other important research centres in Toulouse (e.g. IUCT Oncopole). Moreover, the unit is split between two sites at the INRA and the ENVT campus. Although the two sites are relatively close to each other, they are separated by a river with no nearby bridge, thus it is not possible for the unit staff to meet quickly. A physical connection between these two campuses would improve scientific exchanges. TOXALIM buildings benefited from a recent renovation (lasting two years, 2012-2014) that provided a much better environment and distribution of lab space among teams and technological platforms and acquisition of scientific equipment.

Management team

The management board of the unit is constituted by a head of unit (director of unit, DU) and a deputy head of unit (DHU) each one helped by an assistant. The top management is supported by advisory bodies such as the unit council whose members (9 elected, 8 appointed) represent the different colleges, the general assembly and the team and platform leaders committee. Moreover, the unit has standing committees for various activities (i.e. scientific interaction, seminars, conferences, training and internal competitive funding, equipment, teaching and training, computer needs, protection against radioactive hazards). The administration is under the authority of the DU and is composed by an administrative secretary and a group of unit managers.

HCERES nomenclature

Principal: « SVE Sciences du vivant et environnement » Secondary: « SVE1_LS4 Physiologie, physiopathologie, biologie systémique médicale », « SVE1_LS6 Immunologie, microbiologie, virologie, parasitologie », « SVE2_LS9 Biotechnologies, sciences environnementales, biologie synthétique, agronomie ».

Unit workforce

Unit workforce	Number as at 30/06/2014	Number as at 01/01/2016
N1: Permanent professors and similar positions	16	16
N2: Permanent researchers from Institutions and similar positions	45	43
N3: Other permanent staff (without research duties)	61	62
N4: Other professors (emeritus professor, on-contract professor, etc.)	1	1
N5: Other researchers (Emeritus research director, postdoctoral students, visitors, etc.)	10	11
N6: Other contractual staff (without research duties)	10	12
TOTAL N1 to N6	**143**	**145**

Unit workforce	Number as at 30/06/2014	Number as at 01/01/2016
Doctoral students	31	
Theses defended	34	
Postdoctoral students having spent at least 12 months in the unit	18	
Number of Research Supervisor Qualifications (HDR) taken	3	
Qualified research supervisors (with an HDR) or similar positions	23	29

2 • Overall assessment of the unit

Global assessment of the unit

TOXALIM is a joint research unit (from the merger of 4 INRA units) with the mission of developing research programs in food toxicology. This is the unique and specific mission of TOXALIM at the national level. Since it was created in 2011, excellent scientific results in the field have been obtained that are recognized at both national and international levels. These achievements suggest that this unit will be an important member of the Europe-wide research effort in the field in the next future. TOXALIM is composed of eleven teams and four core technological facilities ("platforms"). The TOXALIM portfolio principally involves research, but also includes important teaching and translational activities. Although there is some heterogeneity in the scientific productivity and international visibility between the different teams, the level of scientific production is excellent with publications in the best scientific journals in the field. The development of toxicology needs a strong interaction with platforms and TOXALIM is well equipped with four technical platforms that play a key role in the global improvement of the research activity of the unit. The development of these platforms to include the most recent technologies is acknowledged by the committee as necessary to tackle new challenges in the field. The unit shows a significant success in obtaining funding, particularly at the national level, despite the reduction in the INRA budget over the last 5 years. There is some heterogeneity in the funding levels achieved by the different teams. In general, it is noted that there is a relatively low participation by most TOXALIM teams in terms of international projects. The research activity benefits from non-permanent staff including students, post-doctoral scientists as well as technicians and engineers hired on contracts. There is a temporal trend towards an increase in the number of non-permanent staff that testifies the team's positive academic reputation and appeal.

Strengths and opportunities in relation to the context

The committee has identified several strengths and opportunities for TOXALIM:

- The major strength of TOXALIM is the convergence of a significant number of well-trained technical/scientific personnel (200 persons), all working on closely related topics in the area of food toxicology (targeted research).
- TOXALIM is characterized by large multidisciplinary research expertise and by a good balance between basic and applied research approaches that are required to address relevant issues in the animal and food safety field.
- The excellent scientific output and the impact on food safety resulting from some of the research at TOXALIM (for instance, the identification of the effects of low doses of bisphenol A (BPA) and the work on the interface between toxicity and metabolism) indicated performance and impact equal to other leading European centres in this field, provided, of course, that the support from INRA and at national level is maintained.
- The technical platforms are another major strength of TOXALIM. They provide the tools (e.g. metabolomics, transcriptomics, animal experimentation) for tackling toxicologically relevant issues. Furthermore, these core facilities possess the capacity to develop new technologies (e.g. miRNA profiling, NGS).

- Some of the Teams possess long-standing and specific expertise (e.g. xenobiotic metabolism, physiology and pathology of the GI tract, hepatic function and PK-PD) that allows a quick targeting of research on relevant dietary contaminants with production of important scientific results.

Weaknesses and threats related to the context

The committee has identified several weaknesses and threats for TOXALIM:

- The teams are heterogeneous in size and strength. This is reflected in the variability in level of international visibility and scientific production, especially in terms of impact, achieved by the different teams.
- Several of the TOXALIM teams are currently working on the same food contaminant (e.g. BPA). While, on one hand, this is a strength because of the relevance of the scientific outcome, on the other hand it may also represent a weakness because research should also be strategically targeted on new and emergent toxicologically relevant food contaminants.
- Although there are a growing number of interactive projects across the different teams of the unit, nevertheless some of the teams need to improve their internal collaborations. The participation of most teams in international projects is relatively low.
- Although the management and organization of TOXALIM is simple and essentially based on one DU and one DHU, together with their assistants, problems of communication appear at all levels: between the division heads and the DU, between the DU and the team's leaders as well as with the rest of the personnel.
- The committee concluded that these problems in communication probably emanate at least in part from the diverse background of the unit. One constituent part derives from two divisions of INRA and the other part from the university and local engineers or veterinary schools. Both bring a different culture, and have a different background. More specifically, the two INRA divisions differ in that they have statutory requirements regarding research topics. A feeling exists that these differences are not sufficiently appreciated.
- Researchers complain of increasing administrative burden.

Recommendations

The committee has the following recommendations for TOXALIM:

- Some of the teams need to be strengthened (i.e. teams 3, 6, 8 and 9). We recommend that the creation of new teams, when dictated by emerging research topics, also takes into account the feasibility of reaching the critical mass required to achieve excellent results.
- The DU is encouraged to improve the cohesion of the unit by further stimulating interactive projects across the unit and to help in the promotion of the international visibility of the researchers.
- Measures should be taken to improve both top-down and bottom-up communication within the unit.
- A concerted effort should be made to promote the further integration between the different constituent parts and cultures in the unit.
- The administrative staff should be reinforced, including staff available to properly assist the teams in both national and internal grant applications. This might increase the willingness of TOXALIM PIs to lead international projects (e.g. Horizon 2020).

3 • Detailed assessments

Assessment of scientific quality and outputs

The main focus of the research of TOXALIM is food toxicology aimed to the characterisation of hazard leading to animal or human chronic diseases. Eleven teams work at this main goal using cell and animal models and techniques spanning from biochemical/cellular assays to “omics”. The variety of technical approaches is also favoured by the presence of 4 technological platforms. In the last 5 years, TOXALIM has produced relevant results in the field (e.g. new findings on the mode of action of known food contaminants and development of new models and assays in toxicology). The main questions currently addressed are the mechanisms of toxicity at low doses of single food contaminants or mixtures during long time exposure and the development of chronic diseases, in particular metabolic disorders such as obesity and diabetes, and cancer. These questions are relevant and in line with the research needs in the field.

The total number of articles of the unit during the last 5 years is 382 almost equally distributed between articles from the unit (first authorship and/or corresponding author from the team and experimental work done in the unit) and in collaboration. What emerges is the excellent scientific production with 18% publications in the top 10%, 63% in the top 25% and 32% in the 25-50% percentile of publications. The mean IF is high for the field (approximately 4 on the 5 year period) and shows a significant increase as compared to the one (approximately 3) of the four research units before the creation of TOXALIM.

Short appreciation on this criterion

The scientific quality and outputs of TOXALIM are excellent, based on the number and quality of scientific publications and based on the quality of the research results. The relevance and novelty of the scientific results of the unit is testified by press release and conferences in different meetings and media as well as by seminal contributions to reports of European/International Agencies. The platforms are instrumental to the quality of the research activity complying with current regulations and quality assurance.

Assessment of the unit's academic reputation and appeal

The scientific recognition and appeal of TOXALIM is testified by its presence in international training networks (Neurogut and Train-ASAP), in the European Training and Teaching board of FELASA, in international risk assessment institutional bodies (e.g. EFSA, IARC) and in the organisation of meetings. Moreover, TOXALIM staff has participated in 149 conferences as invited speakers and have over 100 co-authorships outside France. The number of international grants is good (12) but not all teams have international grants. TOXALIM should lead more international projects (e.g. Horizon 2020).

At the national level TOXALIM researchers are involved either as participants or as coordinators in a large number of projects. AXIOM platform is involved in a national network of metabolomics. The unit’s staff participates in several committees of regulatory agencies, such as ANSES.

Short appreciation on this criterion

The academic reputation and appeal of TOXALIM are very good, based on the international lisibility and on international and national activities of the unit and its different teams, although heterogeneity exists between teams. The number of invitations as speakers in conferences is high as well as collaboration with foreign scientific institutions. Although the number of grants is high, it is not the same for all teams and the number of international projects could be higher.

Assessment of the unit's interaction with the social, economic and cultural environment

TOXALIM staff members are involved in several contracts with companies (33) and industries (6). The investment of the unit in external communication is noteworthy and environmental interaction covers 12% of the activity of the TOXALIM staff. Several scientists are experts at EFSA, IARC and ANSES. Three patents were produced in the last 5 years. Moreover, researchers of the unit give a remarkable number of seminars to non-academic audiences (77) and interviews in newspapers, magazines and TV.

Short appreciation on this criterion

The interaction of TOXALIM with the social, economic and cultural environment is excellent, based on strong partnerships with companies and industries, and based on a high activity of scientific expertise and of external communication to non-scientific public. It is recognized the presence of TOXALIM staff as experts in national and international risk assessment agencies as well as the participation to conferences in non-academic structures and to a significant number of interviews for newspapers, national radios and TV.

Assessment of the unit's organisation and life

TOXALIM involves the work of 200 persons, more than 50% with permanent positions. These positions are almost equally distributed between full time researchers and professors (39%), engineers (23%) and technicians. However, these positions are not equally distributed within the different teams creating some critical situations. These have been highlighted in this report (see detailed assessment of the teams).

The TOXALIM activity profile involves as several major components: research (53%) and teaching through research (24%). Environmental interaction (i.e. translational research) and support (i.e. participation to scientific committees) involve 12% and 11% of the activity, respectively. This distribution of the efforts occurs within the teams although some imbalance has been identified (see detailed assessment of the teams).

Although the Committee acknowledges that the promotion of interactions between different teams has occurred during the last 5 years, the scientific collaboration between teams is very heterogeneous (ranging from very good as for team 1 to limited as for team 8). There remains some margin for improvement.

Overall, the level of communication between the DU and the personnel is not entirely effective. The personnel complains that there is limited discussion of the scientific decisions and planning with the DU while the DU listed numerous occasions when staff were invited to participate. The committee recommends that actions should be taken to improve two-way communication within the unit. Common efforts from the staff and the direction of the unit (DU, DHU, team leaders) should be done to solve this problem. The interaction with managing bodies should be improved as well.

Short appreciation on this criterion

The unit's organisation and life are good. However, there is one critical point (i.e. communication with all staff members) that impacts negatively on the unit's life that must be significantly improved. This concerns every staff member including team leaders, the DU and the DHU. In addition to that, internal collaborations between at least some teams should be improved.

Assessment of the unit's involvement in training through research

Apart from their core involvement in research activities, Professors and other staff from each team in TOXALIM also have a significant involvement in teaching. This is manifested mostly in terms of master's courses, training at the Agronomy and the Veterinary "High Schools" and teaching at the University of Toulouse. TOXALIM is also part of the "Écoles Doctorales" (PhD Colleges) of 458 SEVAB (Sciences écologiques, vétérinaires, agronomiques et bioingenieries) and 151 BSB (Biology, Health and Biotechnologies).

The research activity of the unit benefits from non-permanent staff, including students and post-doctoral scientists. There is a trend towards an increase of the number of students/post-docs, particularly in the number of post-docs (from 6 in 2012 to 10 in 2013) that testifies the unit's academic reputation and appeal.

The committee had a meeting with Mr Claude MARANGES, director of the doctoral school 458 SEVAB, and Mr Philippe VALET, director of the doctoral school 151 BSB. The majority of the students at TOXALIM belong to these two schools. Both directors agreed on the high level of training provided by TOXALIM. They recognized that the unit has a clear commitment in the doctoral schools with members on the boards of both schools. Most of the students in TOXALIM seem to achieve their PhD within the three-year limit. If required, a fourth year registration is generally allowed, providing the unit has the required funding. Generally, TOXALIM conforms to the doctoral school rules with a maximum average per team of 2 concurrent PhD candidates per HDR-qualified staff member.

The committee had also a meeting with the PhD students/post-docs of the unit. The majority of the PhD students enrolled in the unit are registered at the SEVAB doctoral school although a minority are registered at the BSB school. The PhD students and Post-Docs enjoy the scientific life within the teams and the access at the platforms that

they recognize to be of great help in the progress of their research project. The students see the achievement of the PhD within three years as a difficult goal. Therefore, they wish for a better monitoring of the progress of their research activity during the three-year time and for a timely search of funding for the possible fourth year registration. Regular (once a year) meetings of the "thesis committee" (student, his/her supervisor at the unit, a representative of the doctoral school, plus external people) guarantee the interaction between the research team and the doctoral school. However, the students perceive a lack of visibility, due to their status as non-permanent staff within the unit, and also of the unit per se at national level, which they fear might hamper their future job opportunities. They report limited participation at events open to the general scientific community of TOXALIM, and possibly to a broader national scientific audience, where they could present and discuss the results of their research projects. The Committee invites the director of TOXALIM as well as the student supervisors to promote the creation of a closer network among students by providing more opportunities for scientific events involving all the students working in TOXALIM. This issue may also relate in part to the matter of bi-directional communication within TOXALIM.

Short appreciation on this criterion

The unit's involvement in training through research is very good, based on TOXALIM involvements in master's courses, training at the agronomy and the veterinary "high schools", teaching at the University of Toulouse and activities in two doctoral schools (numbers 458 and 151). Teaching represents 24% of the activity profile of TOXALIM. Professors involved in research play also a major role in Master's and PhD's organization and the staff of the teams is largely involved in the training of students for technical graduation (BTS), master degree and PhDs.

Assessment of the strategy and the five-year plan

The strategic plan for next 5 years (2016-2020) presents as a common goal the characterization of the mechanisms of action of food contaminants singly and in mixtures (pesticides, endocrine disruptors, toxins, nanoparticles, veterinary drugs) and the identification of biomarkers of exposure/effect in body fluids or organs at early stage of dysregulation to prevent toxic effects. The skills of TOXALIM in patho-physiology, cell biology, molecular biology and analytical chemistry will be used to address this general objective. It is recognised that the "omics" approaches should be increased as well as the integration of biostatistics and bioinformatics expertise. There is growing interest in nutrition and disease research on the impact of the gut microbiota in food toxicology and TOXALIM has the expertise to tackle these emerging topics that will be a strategic goal for the next 5 years. Alternative cell models (e.g. *in vitro* gut barrier, 3D culture) will be developed and used to improve the knowledge of the mechanisms of toxicity. It is recognised that there is a need to develop toxicological epigenomics. The platforms will face new technological challenges (AXIOM will develop MS imaging; TRIX NGS and epigenetic techniques, M2C tissue and 3D cell imaging; EZOP embryo conservation and zebra fish).

The strategic plan combines fields of expertise of the unit (essential for the feasibility and quality of research that will be carried out) and the development of new expertise that will allow tackling challenging topics in the field. There is a good equilibrium between feasibility and risk. The committee identifies one topic that is currently not considered in the strategic plan and that deserves further analysis: neurotoxicity, which is emerging as a sensitive critical effect for low doses toxicants.

Besides basic research expertise, the unit includes experts in more applied aspects that are critical to respond to societal challenges (expertise and advice to authorities and stakeholders). The committee recommends that this is taken into consideration in the strategic plan and distribution of workforce and budget.

It is recommended that the unit formulates a clearer mission statement which should also explicitly include the statutory tasks of parts of the unit. Furthermore, it is concluded that there is a lack of explicit targets that would help outside assessment and help the unit and teams self-evaluation. This goes for most criteria, but as an example, concerning publications, the expected minimum ratio of high impact factor publications per senior researcher per year could be set optimistically to encourage further ambition.

Short appreciation on this criterion

The strategy and the five-year plan are excellent based on a good combination of existing expertise (essential for the feasibility and quality of the future research) and the development of new expertise (needed for new challenges). One of the major strength of TOXALIM, i.e. the large multidisciplinary research expertise, allows the implementation of ambitious research projects addressing the major issues in food toxicology. Besides basic research, more applied aspects needed to respond to societal challenges (including advice to authorities and stakeholders) deserves recognition and support.

4 • Team-by-team analysis

Team 1: Integrative Toxicology et Metabolism (TIM)

Name of team leader: Mr Hervé GUILLOU

Workforce

Team workforce	Number as at 30/06/2014	Number as at 01/01/2016
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	6	5
N3: Other permanent staff (without research duties)	3	3
N4: Other professors (PREM, ECC, etc.)		
N5: Other researchers (DREM, Postdoctoral students, visitors, etc.)	2	1
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**11**	**9**

Team workforce	Number as at 30/06/2014	Number as at 01/01/2016
Doctoral students	2	
Theses defended	5	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken	2	
Qualified research supervisors (with an HDR) or similar positions	2	3

•Detailed assessments

Assessment of scientific quality and outputs

The research activity of the team is essentially focused on the molecular mechanisms of nuclear receptors involved in the sensing of xenobiotics and lipids (CAR, PXR, PPARs, LXRs) on hepatic physiology. Given the size of this young team, scientific production since 2009 is excellent: 52 articles were published with a mean IF equal to 5 (25% in the first Quartile). The number of peer-reviewed publications with IF per N2 researchers is 11.7 over the last 5 years. As demonstrated by the list of publications involving internal or external collaborations (43 out of 52, 83%), the expertise of this team is widely recognized. However only few of the published papers (9 out of 52, 17%) result from works within the team and 16 publications are from newly integrated members. Particularly, we retain excellent publications in scientific journals in the field (*Hepatology*, IF 11.5; *J. Hepatol*, IF 9.5).

Short appreciation on this criterion

Regarding the size of this young team, the production is excellent based on the number and quality of scientific publications, although a great number of papers are from new members in the team. This is due to the originality of their research in the sensing of xenobiotics and lipids on hepatic physiology. The expertise of the team is also attested by a high number of publications involving internal or external collaborations.

Assessment of the team's academic reputation and appeal

The expertise of this team is excellent and widely recognized as highlighted by the invitations for a significant number of international (12) and national conferences and seminars (18). Since 2009, the team is also involved in the organization of 1 international and 2 national meetings. In addition, several scientists of the team received prize or distinction during the past period.

The team's academic reputation and appeal is also proved by the high number of PhD students (9) given the number of qualified research supervisors with an HDR (2). In addition, the number of master-level students is significant (13). The ability to raise funds is excellent. The number of international (3) and national (14) grants is impressive and they demonstrate a dynamic activity and most of them are obtained in collaboration (10), 2 ANR projects, 1 industrial project, 1 ANSES project and 3 regional projects were directly coordinated by the team.

Short appreciation on this criterion

The team academic reputation is outstanding based on its ability to raise funds and to attract new people. It is also highlighted by the invitations for many conferences and by awards received by different members of the team. The team shares its expertise for agencies, developped collaboration with the academic world and industrial partners and is able to attract a high number of students.

Assessment of the team's interaction with the social, economic and cultural environment

The interaction of the team with the social and economic environment is excellent. In particular, the team is in link with local (Arterris, Vaiomer and Physiogenex), national (Lesaffre) or international (Actigenomics) industrial partners. In addition, the investment of the team in external communication is noteworthy with many conferences and seminars with the general public, and with many interviews in magazines or in the TV.

The team members are also: 1) involved in many expertise for public bodies (international or national); 2) in scientific committees (international, national, university and INRA); 3) in editorial board of international scientific journals; 4) involved in the evaluation of scientific projects.

Short appreciation on this criterion

The team interaction with the social, economic and cultural environment is excellent based on its links with many partners (local, French or international companies) and thanks to its high level of communication to the general public. The members of the team are also clearly involved in valorisation of their research through various expertises for public bodies, participation in scientific committees, editorial board activities and evaluation of scientific projects.

Assessment of the team's involvement in training through research

The involvement of the team in training through research is very high. The team has trained 9 PhD students (6 defended and 3 in progress) and 1 post-doctoral fellow in the past four years. In addition, 3 master-level students are supervised each year. Given the small number of qualified research supervisors with an HDR (2), it’s excellent. However, some scientists might defend their HDR.

The involvement of the team members in teaching activities is limited (29 h annually). However, the team leader initiated and is in charge of the “pre-clinical toxicology” teaching at the M2R “Pharmacological Innovations” of the University of Toulouse.

Short appreciation on this criterion

The involvement of the team in training through research is excellent. Due to their high visibility and their very good production, the team is appealing for students. The originality of their work is also attractive. However, to reinforce this criterion, the team needs to increase its HDR number.

Assessment of the strategy and the five-year plan

The five-year plan is fine. It is in line with the past activities and focus on hepatic toxicology and physiology. As in the past period, the majority of the project is based on a strong collaborative network, especially with different teams and platforms of the unit. The project concerning the lipids in hepatotoxicology, the function of PPARs in the hepatocytes, and the roles of xenobiotic receptors in energy homeostasis are clearly in line with the previous mentioned. The contribution of microbiota metabolites to the host physiology and those concerning the profiling of the effects of food contaminants alone or in mixtures constitute new research projects based on the recent recruitment of two scientists (Ms Sandrine ELLERO-SIMATOS and Ms Laurence GAMET-PAYRASTRE).

Short appreciation on this criterion

The team strategy is excellent. The new five-year plan developped by the whole team is in line with the past activities and focus on hepatic toxicology and physiology. The projects are ambitious and original. This should contribute to maintain their high visibility and attractiveness.

Conclusion

The Integrative Toxicology and Metabolism (TIM) team is a small group with 4 researchers. This team had an excellent scientific production and shows a high number of fruitful collaborations with national and international laboratories. The expertise of this team is excellent and widely recognized. In addition, its ability to raise funds is excellent. The research program is coherent and original, and in line with the previous period. The involvement of the team in training through research is excellent. The team is managed by a young researcher and seems to be very dynamic.

- Strengths and opportunities:

The main strengths of this team are:

- high number of fruitful collaborations with national and international laboratories;
- strong interactions with others teams and platforms of the unit;
- good expertise of the team;
- obtaining many grants in national and international collaborative projects as participant or coordinator;
- a young and active team leader;
- a coherent research program;
- an excellent rate of PhD students (6 defended and 3 in progress).

- Weaknesses and threats:

The main weaknesses of this team are:

- significant risk of dispersion between the projects led in collaboration and those developed by the own team (see rate of publications);
- limited teaching activities.

- Recommendations:

In the past years the team developed numerous and fruitful collaborations, and obtained lot of grants. However, this strategy should not be detrimental to the internal research development. The team leader is thus prompted to pay attention to the balance between the external/internal research projects.

Team 2: Metabolism of Xenobiotic (MeX)

Name of team leader: Mr Daniel ZALKO

Workforce

Team workforce	Number as at 30/06/2014	Number as at 01/01/2016
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	6	6
N3: Other permanent staff (without research duties)	6	5
N4: Other professors (PREM, ECC, etc.)		
N5: Other researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)	1	1
TOTAL N1 to N6	**13**	**12**

Team workforce	Number as at 30/06/2014	Number as at 01/01/2016
Doctoral students	6	
Theses defended	4	
Postdoctoral students having spent at least 12 months in the unit	4	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	2	3

•Detailed assessments

Assessment of scientific quality and outputs

The research activity of the team is essentially focused on the ability of living organisms to metabolize xenobiotics which are potentially harmful chemicals as endocrine disrupting chemicals (EDCs), brominated flame retardants (BFRs) and perfluorinated compounds (PFCs). Since 2009, the scientific production of the team (6 full-time researchers), has been excellent: 69 articles were published with a mean IF around 4.5 (26% in the first Quartile). The number of peer-reviewed publications with IF per N2 researchers is 11.7 over the last 5 years. As demonstrated by the list of publications involving internal or external collaborations (32 out of 69, 46%), the expertise of this team is widely recognized. The results of the team (37 out of 69, 54%) are published in excellent journals. Most of the excellent publications are in scientific journals within the field (*Environ Health Perspect*, IF 7, 6; *J Toxicol Environ Health B Crit Rev*, IF 5.4) or in more generalist journals (*Nucleic Acid Research*, IF 8, 3).

Short appreciation on this criterion

Regarding the size of the team, the production is excellent based on the number and quality of scientific publications. This is due to the originality of their research on the capability of living organisms to metabolize xenobiotics which are potentially harmful chemicals as endocrine disrupting chemicals (EDCs), brominated flame retardants (BFRs) and perfluorinated compounds (PFCs). The expertise of the team is also attested by a high number of publications involving internal or external collaborations.

Assessment of the team's academic reputation and appeal

The expertise of this team is excellent and widely recognized as highlighted by the invitations for a significant number of international (17) and national conferences and seminars (18). Since 2009, the team has also been involved in the organisation of 3 international and 2 national meetings. In addition, several scientists of the team are involved in expert panels from national and international food safety agencies.

The team's academic reputation and appeal is also proved by the high number of PhD students (10) and Post-doctoral students (4) given the number of qualified research supervisors with an HDR (2). In addition, the number of master-level students is significant (14).

The ability to raise funds is excellent. The number of international (7), national (34) and INRA (5) grants are very impressive and they demonstrate a strong dynamic activity. Most of the grants were obtained in collaboration (30), 3 international projects, 4 ANSES projects, 1 Post-Grenelles project, 5 industrial projects and 3 INRA projects were directly coordinated by the team.

Short appreciation on this criterion

The team academic reputation is outstanding based on its ability to raise funds and to attract new people. It is also highlighted by the invitations for many conferences and the involvment in scientific animation (organisation of meetings and chair of scientific session). The team shares its expertise for agencies, developped collaboration with the academic world and industrial partners and is able to attract a high number of students.

Assessment of the team's interaction with the social, economic and cultural environment

The interaction of the team with the social and economic environment is excellent. The investment of the team in external communication is noteworthy with many conferences and seminars with the general public, and with many interviews in magazines, radio or in the TV.

The team members are also: 1) involved in many expertise for public bodies (international or national); 2) in scientific committees (national and INRA); 3) involved in the evaluation of scientific projects (international and national).

Short appreciation on this criterion

The team interaction with the social, economic and cultural environment is excellent based on its links with many partners (local, French or international companies) and thanks to its high level of communication to the general public. The members of the team are also clearly involved in valorisation of their research through various expertises for public bodies, participation in scientific committees and evaluation of scientific projects.

Assessment of the team's involvement in training through research

The involvement of the team in training through research is very good. The team has trained 10 PhD students (7 defended and 3 in progress) and 4 post-doctoral fellows in the past four years. In addition, 3 master-level students are supervised each year. Given the small number of qualified research supervisors with an HDR (2) this is excellent. However, some scientists might defend their HDR. The involvement of the team members in teaching activities is limited (40 h/annually). However, team members are in charge of teaching at the M2R level in Toulouse and Paris, and at the PhD level in Brazil.

Short appreciation on this criterion

The involvement of the team in training through research is excellent. Due to their high visibility and their very good production, the team is appealing for students. The originality of their work is also attractive. However, to reinforce this criterion, the team needs to increase its HDR number.

Assessment of the strategy and the five-year plan

The five-year plan is in line with the past activities and focus on the metabolic effects of food contaminants, in particular the impact on health of mixtures of pesticides, at concentrations which can be made available through food to consumers. The goal is to understand the cellular effects, mechanisms of action and seeking biomarkers of exposure. As in the past period, the majority of the project is based on a strong collaborative network. In addition, most of them are already received financial support.

Short appreciation on this criterion

The team strategy is excellent. The new five-year plan developed by the whole team is in line with the past activities and focus on the metabolic effects of food contaminants in the goal to understand the cellular effects, mechanisms of action and seeking biomarkers of exposure. The projects are ambitious and original. This should contribute to maintain their high visibility and attractiveness.

Conclusion

The Metabolism of Xenobiotics (MeX) team is an average size group with 6 researchers. This team had an excellent scientific production and shows a high number of fruitful collaborations with national and international laboratories. The expertise of this team is excellent and widely recognized. In addition, his ability to raise funds is impressive. The research program is coherent and original, and in line with the previous period. The involvement of the team in training through research is very good. The team seems to be very dynamic.

- Strengths and opportunities:

The main strengths of this team are:

- high number of fruitful collaborations with national and international laboratories;
- strong interactions with others teams and platforms of the unit;
- very Good expertise of the team;
- obtaining many grants in national and international collaborative projects as participant or coordinator;
- the research program is coherent;
- an important rate of PhD (6 defended and 3 in progress) and post-doc students (4).

- Weaknesses and threats:

The main weaknesses of this team are limited teaching activities and limited number of HDR-trained staff.

- Recommendations:

In the past years the team developed numerous and fruitful collaborations, obtained lot of grants and trained numerous PhD students. However, the number of qualified research supervisors with an HDR is low (2). The young researchers should pass the HDR.

Team 3: Endocrines Disrupting Pesticides (PEP)

Name of team leader: Ms Catherine VIGUIÉ

Workforce

Team workforce	Number as at 30/06/2014	Number as at 01/01/2016
N1: Permanent professors and similar positions	2	2
N2: Permanent EPST or EPIC researchers and similar positions	1	1
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other researchers (DREM, Postdoctoral students, visitors, etc.)	0.5	
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**4.5**	**4**

Team workforce	Number as at 30/06/2014	Number as at 01/01/2016
Doctoral students	2	
Theses defended	3	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	3	3

•Detailed assessments

Assessment of scientific quality and outputs

The research activity of the team is essentially focused on the development and the validation of relevant models for the human in order, to evaluate the effects of endocrine disruptors. The aim of the team is to investigate endocrine disruptors. Since 2009, the scientific production of this small team (1 full-time researcher and two university professors with heavy teaching duties) has been excellent: 23 articles with a mean IF up to 4 (25% in the first Quartile) and 10 book chapters were published. The number of peer-reviewed publications with IF per N1 and N2 researchers is 7.7 over the last 5 years. As demonstrated by the list of publications involving internal or external collaborations (9 out of 24, 37%), the expertise of this team is widely recognized. The results of the team (15 out of 24, 63%) are published in excellent journals. Particularly, the committee noted excellent publications in scientific journals in the field (*Environ Health Perspect*, IF 7, 6; *Toxicology*, IF 4,8) or in more generalist journals (*Endocrinology*, IF 4,8).

Short appreciation on this criterion

Regarding the size of the team, which is small, the production is excellent based on the number and quality of scientific publications. This is due to the originality of their integrative approaches to the evaluate the endocrine disruptors and their mechanisms of action. The expertise of the team is also attested by numerous publications involving internal or external collaborations.

Assessment of the team's academic reputation and appeal

The team academic reputation and appeal is excellent. The expertise of this team is excellent and recognized as highlighted by the invitations for a significant number of international (3) and national conferences and seminars (2).

The team's academic reputation and appeal is also proved by the high number of PhD students (4) and Post-doctoral scientist (1) trained given the small number of full-time equivalent researcher (2). In addition, the number of veterinary thesis and master-level students is significant (13). Two PhD research works received an award during the past period. The team is co-coordinator of a working group “Reproduction and environment” of the GDR REPRO 3606.

The ability to raise funds is very good. The number of national (7) and INRA (4) grants are impressive and they demonstrate a strong dynamic activity. In addition, most of the grants were directly coordinated by the team (8/11).

Short appreciation on this criterion

The team academic reputation is excellent based on its ability to raise funds. It is also highlighted by the invitations to many conferences and the involvement in scientific animation (chair of scientific session and participation to scientific and organizing committee). The team shares its expertise for agencies, developed collaboration with the academic world and industrial partners and is able to attract a high number of students.

Assessment of the team's interaction with the social, economic and cultural environment

The interaction of the team with the social and economic environment is excellent. Several members of the team are involved in different expertise for public bodies. In addition, the investment of the team in external communication is noteworthy with many reports in technical and professional reviews, several conferences and seminars with the general public, and with several interviews in magazines, radio or in the TV.

The team members are also: 1) involved in many expertises for public bodies (international or national); 2) in scientific committees (university and INRA); 3) involved in the evaluation of scientific projects.

Short appreciation on this criterion

The interaction of the team with the social and economic environment is excellent. The investment of the team in external communication is noteworthy with many conferences and seminars with the general public, and with many interviews reports in technical and professional reviews. The members of the team are also clearly involved in valorisation of their research through various expertises for public bodies, participation in scientific committees and evaluation of scientific projects.

Assessment of the team's involvement in training through research

The involvement of the team in training through research is excellent. The team has trained 5 PhD students (3 defended and 2 in progress) and 1 post-doctoral fellow in the past four years. In addition, 3 veterinary thesis or master-level students are supervised each year. The team is strongly involved in teaching activities. In particular, the two university professors have heavy teaching duties in the Veterinary School. However, the full-time researcher is also in charge of teaching in the veterinary school (20h/year).

Short appreciation on this criterion

The involvement of the team in training through research is excellent. Due to their high visibility and their very good production, the team is appealing for students. The originality of their work is also attractive.

Assessment of the strategy and the five-year plan

The five-year plan is excellent. It is in line with the past activities and focus on effects of fetal exposure to Bisphenol A. The project is based on an integrative approach to understand and predict the deleterious effects on fetal development. As in the past period, the project will be done with internal collaboration. In addition, this project has already received financial support.

Short appreciation on this criterion

The team strategy is excellent. The new five-year plan developped by the whole team is in line with the past activities and focus on the evaluation of endocrine disruptors and their mechanisms of action through the development of integrative approaches. The projects are ambitious and original. This should contribute to maintain their high visibility and attractiveness.

Conclusion

The Endocrines Disrupting Pesticides (PEP) team is a very small group with one full-time researcher and two university professors involved in teaching (2 full-time equivalent researchers) and one technician. This team had an excellent scientific production and shows a high number of fruitful collaborations. The expertise of this team is excellent and widely recognised. In addition, the team's ability to raise funds is impressive. The research program is coherent and original, and in line with the previous period. The involvement of the team in training through research is excellent. The team seems to be very dynamic.

- Strengths and opportunities:

The main strengths of this team are:

- transversal and key positioning within unit;
- obtaining many grants in national projects as participant or coordinator;
- the research program is coherent and in adequacy with the social demand;
- capacity to work on different animal models.

- Weaknesses and threats:

The main weaknesses of this team are its small size and the high medium age of its members (52 years).

- Recommendations:

Given the small size of the team and the age of the scientists, the team should be reinforced by the recruitment of at least one young researcher.

Team 4: Neuro-Gastroenterology and Nutrition (NGN)

Name of team leader: Ms Vassilia THÉODOROU

Workforce

Team workforce	Number as at 30/06/2014	Number as at 01/01/2016
N1: Permanent professors and similar positions	2	2
N2: Permanent EPST or EPIC researchers and similar positions	4	4
N3: Other permanent staff (without research duties)	8	8
N4: Other professors (PREM, ECC, etc.)		
N5: Other researchers (DREM, Postdoctoral students, visitors, etc.)	2	2
N6: Other contractual staff (without research duties)	2	1
TOTAL N1 to N6	**18**	**17**

Team workforce	Number as at 30/06/2014	Number as at 01/01/2016
Doctoral students	1.5	
Theses defended	4.5	
Postdoctoral students having spent at least 12 months in the unit	4	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	2	2

Detailed assessments

Assessment of scientific quality and outputs

The research is focused on various aspects of the intestinal barrier function. In particular the topics under study are: i) the influence of endoluminal factors on gut barrier function and viscerosensititvity; ii) the influence of estrogen and estrogen-like compounds of natural or chemical origin on intestinal homeostasis and diseases and, iii) the brain-gut interplay and intestinal barrier functions in relation to their mechanism and pathophysiological consequences. This team has brought significant contribution to the field of IBD (inflammatory bowel diseases) and IBS (irritable bowel syndromes). The effect of phytoestrogens on models mimicking IBS and IBD has also been studied and an important contribution has been the demonstration that bisphenol A (BPA) affects intestinal barrier functions. Moreover, the studies on the brain-gut interaction are important and innovative.

Since 2009, the scientific production of the team (6 full-time researchers and 2 university professors involved in teaching duties) has been excellent: 43 articles were published with a mean IF around 5 (33% in the first Quartile).

In the period of the report there were 8 permanent (N1 and N2) positions, since also Mr Eric HOUDEAU and Ms Laurence GUZYLACK-PIRIOU were part of the team 4. Therefore, the mean number of articles published/permanent positions is 8.9 over the last 5 years. As demonstrated by the list of publications involving internal or external collaborations (46 out of 75, 61%), the expertise of this team is widely recognized. The team results are published in excellent journals (29 out of 75, 39%). Particularly, they have some excellent publications in scientific journals in the field (*Gastroenterology*, IF 12,9; *Am J Gastroenterol*, IF 8; *Pain*, IF 6,3) or in more generalist journals (*Proc Natl Acad Sci USA*, IF 10,7; *FASEB J*, IF, 6).

Short appreciation on this criterion

This is a large team of scientists working on several aspects of the intestinal barrier function. The topics investigated are only partially known and therefore research in the field is important. The team made significant contributions to the knowledge of intestinal barrier functioning and on the relation between gut and brain. Most of the publications are in journals with high impact factor and have a very good citation index. Many of the papers, although only recently published, have already been cited many times.

In summary the scientific quality and outputs of the team are excellent.

Assessment of the team's academic reputation and appeal

The team has been and is involved in several projects. In fact, members are partners of the European Training in Neural Regulation and members of an European network program (Neurogut). Moreover, they are partners in International, national and regional grant projects.

They received grants from regional and national agencies as well as industrial grants. The researchers have been involved in the organization of national meetings. They are members of national (French) scientific boards and councils such as the Société Française de Nutrition, Institut Carnot Qualiment, Groupe Français de Neurogastroenterologie, Club d'études des cellules épithéliales digestives.

The team is also involved in teaching activity (3 full professors). Teaching activity is in Masters (Food safety and quality, Pharmacology innovation, preclinical toxicology) and Doctorate school.

Short appreciation on this criterion

The team's academic reputation and appeal are very good as can be seen by the involvement of the members in several international and national projects, as well as their involvement in National scientific boards and councils. Another point in favour of their reputation is the integration of 3 new researchers and a six month associate professor in the team. Moreover the research of the team has been published in journals with a good IF. In conclusion, the team's academic reputation and appeal are very good.

Assessment of the team's interaction with the social, economic and cultural environment

The researchers act as experts in international agencies (JPI "a healthy diet for a healthy life"; ILSI Europe). They also have active collaborations with industrial partners leading to PhD CIFRE (Conventions Industrielles de Formation par la Recherche) (industrial agreement of training through research) as well to a permanent position in the team for a researcher from the industry. Patent exploitation is also reported. They also collaborate with international partners (Universities in USA (Chicago), Hungary, Italy). Interaction with the society through 12 seminars, conferences, professional reviews and participation in both national and local events ("Salon de l'agriculture", "Nuit des chercheurs") is also reported.

Short appreciation on this criterion

Team's members are experts for international bodies. They have industrial collaborations with academic input (PhD, post-doctoral students, a permanent position; patent exploitation). Active international academic collaborations is also present. The collaboration with clinicians should be strengthened. Interaction with the society through seminars, conferences also for the general public (magazine/newspapers, radio TV) is also reported. Therefore, the team's interactions with the social, economic and cultural environment are very good.

Assessment of the team's involvement in training through research

The team is composed of three full professors, teaching in various courses such as Master's (food safety and quality, pharmacology innovation, preclinical toxicology) and doctorate school.

From 2009 until now the team trained 8 PhD students and 4 post-docs. A member of the team is deputy at SEVAB (sciences, ecology, veterinary, agriculture, biology) PhD college. Teaching activity also involves teaching in Engineer school of Purpan (EI-Purpan), M2 Toulouse 3 and DIU "explorations fonctionelles digestives".

Short appreciation on this criterion

Members of the team teach in Doctorate school as well as in Engineer school of Purpan (EI-Purpan), M2 Toulouse 3. Several PhD students and post-docs have been trained within the team. Therefore, the team's involvement in training through research is very good.

Assessment of the strategy and the five-year plan

Projects for the next five years are quite in line with the field of research proper of the team. Specific expertise by new researchers that joined the team will be important in pursuing some of the aims planned for 2016-2020. Three main aspects will be developed: axis 1: Influence of endoluminal proteases on intestinal mucus secretion and epithelial-mucus barriers cross talk. Part of this research will be carried out in planned foreseen with a PhD student in common between the two units. The proposed research is in line with the expertise of the team and therefore perfectly feasible. No mention of funds for this axis. Axis 2: Microbiota modulation in early or adult life: pathophysiological consequences. This part is also perfectly in line with the expertise of the team; part will carried out in collaboration with team at INSERM Toulouse and within the frame of the ITN Neurogut European network (one PhD student). Industrial partnership between the institut-rosell-lallemand.com (probiotic producers) and Nestlé, is predicted. Axis 3: Brain-gut interplay: pathophysiological consequences. The possibility that various types of stress may affect the propensity to develop low-grade inflammation diseases (various metabolic diseases), it is intriguing and has not been well investigated in past. The topic is again in line with the field of research proper of the team. Also the converse link, that is, the effect of alteration in the gut intestinal barrier on emotional behaviour and BDNF levels will be investigated. The topics are very interesting. The funding for these researches is not mentioned.

Short appreciation on this criterion

Given the expertise of the researchers, the planned projects, in line with the field of research of the team, are absolutely feasible. Moreover, the specific expertise by new researchers that joined the team will be important in pursuing some of the aims planned for 2016-2020. In summary, the strategy and the five-year plan are excellent.

Conclusion

This is a large team of scientists working on several aspects of the intestinal barrier function. This field of research is relatively new and the team made significant contributions to it.

- Strengths and opportunities:

This is a large team with many experienced researchers in the top level of their own field.

- Weaknesses and threats:

The team has been split into two (team 11 with 4 people leaving). Also, two members of the team are now retired and will act as emeriti.

- Recommendations:

The key skills of each member of the team should be better exploited.

The collaboration with clinicians should be strengthened.

Team 5: Biosynthesis and toxicity of mycotoxins

Name of team leader: Ms Isabelle OSWALD

Workforce

Team workforce	Number as at 30/06/2014	Number as at 01/01/2016
N1: Permanent professors and similar positions	1	2
N2: Permanent EPST or EPIC researchers and similar positions	1	1
N3: Other permanent staff (without research duties)	6	5
N4: Other professors (PREM, ECC, etc.)		
N5: Other researchers (DREM, Postdoctoral students, visitors, etc.)	3	1
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**11**	**9**

Team workforce	Number as at 30/06/2014	Number as at 01/01/2016
Doctoral students	8	
Theses defended	7	
Postdoctoral students having spent at least 12 months in the unit	6	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	3	4

•Detailed assessments

Assessment of scientific quality and outputs

The team works on the biosynthesis, toxicology and pathophysiology of mycotoxins. The emphasis is on feed safety, but is highly relevant for humans too. The problems associated with mycotoxins seem to become even more relevant with the current climate change, which appears to predispose to increased mycotoxins in cereal crops. In their research, the team spans a spectrum from the *in vitro* cellular level to the animal, with an emphasis on the effects on the intestines, and the wider (immunological) consequences thereof. This also involves the possible additive and synergistic effects between different mycotoxins, and the detection of new and masked mycotoxins. Another part involves reduction of toxins present by inactivation strategies, and prevention of biosynthesis of toxic metabolites in plants.

The team has a very good standing in the international scientific world, as is evident from the number of publications in high ranking international peer reviewed journals, and the number of citations per paper. The number

of peer-reviewed publications with IF per N1 and N2 researchers is 31 over the last 5 years, which is excellent. The scope of the research is quite wide as mentioned above, and is focussed on plant and animal, not human. It is most original 1. in its emphasis on the intestine, which central position in the immunological system is more and more appreciated, and 2. in working towards new preventative strategies in plants.

Short appreciation on this criterion

The team belongs to the international top in this field, and can be described as excellent for the number of publications in high ranking international peer reviewed journals and for the relevance and originality of the research activity.

Assessment of the team's academic reputation and appeal

Members of the team are regularly invited to speak at international conferences (though it concerns mainly one person), and (co-)organised national congresses, and are editorial members and reviewers at reputed international journals. The team has attracted 30 research projects, including 3 European projects, 7 national ANR projects, and 8 with industry. It has also attracted 4 visiting foreign professors, and 23 temporary scientists and (PhD-) students. Furthermore, team members sit in a total of 16 scientific councils of which 3 international.

Short appreciation on this criterion

The team's quality is consistent with an excellent academic reputation and appeal as testified by the invitation to international conferences, number of research projects including international ones and presence in the editorial board of international journals and scientific councils.

Assessment of the team's interaction with the social, economic and cultural environment

There is a good interaction with industrial partners and technical institutes by giving seminars and papers in technical and professional journals. This will ensure the dissemination of knowledge to the (feed) industry. A weak point is the low frequency of dissemination of knowledge to the general public on such an important and relevant subject. Furthermore, exploitation of the knowledge obtained through patents etc. should be increased.

Short appreciation on this criterion

The very good interaction with the industrial environment does not lead to visible valorisation. The contact with the general public should be improved.

Assessment of the team's involvement in training through research

The team had successful 8 PhD defences between 2009 and 2014, and has currently 9 PhD students. 42 students have been trained. Furthermore, team members have a strong implication in teaching. In particular, team members are involved in various master and PhD programs, and do also teaching in other part of France as well as internationally.

Short appreciation on this criterion

The team is very active in training through research as judged by the number of PhD theses successfully defended, and the number of current PhD students. Its performance can be characterized as very good.

Assessment of the strategy and the five-year plan

The strategy of the team for the next years is to focus on the identification of hitherto unknown toxic metabolites in crops, and on preventive measures against contamination. This is an original and practical approach, and does not carry much risk. It can be anticipated that many new compounds will be identified and will lead to publications, as well as practical methods for rapid and sensitive detection. The second tier of prevention especially is scientifically as well as practically sound, and allows for publications, cooperation with industry, applications and likely patents, thus showing a good link between basic and applied research. Most if not all of the equipment and expertise is present or can be accessed through the network of the team. This means that the feasibility of the

approach is high. It apparently also means that the emphasis is taken off from the higher risk transcriptomics approach.

Short appreciation on this criterion

An excellent, scientifically and practically sound strategy and 5-year plan fitting with the team's quality is recognised. The approach is original and feasible and the probability of achieving the objectives is high based on the scientific excellence of the team, network of collaborations and successful funding of projects.

Conclusion

The research is focused on a highly relevant topic in food toxicology and the team has a strong national and international recognition. Success is expected in achieving the objectives of the future 5 year strategic plan.

- Strengths and opportunities:

The team is one of the leaders in the field. It is well equipped to deal with the challenges posed, and where not, to attract relevant expertise. A solid, practical, and feasible strategy has been proposed for the next years.

- Weaknesses and threats:

There is limited exploitation (in terms of patents) of the work, and little contact with the general public. Furthermore, in several areas such as (but not limited to) invited international speaker there is too much reliance on one person (the team leader).

- Recommendations:

Clear(er) targets should be set for all performance indicators (for instance publications per senior researcher, etc.), in order to monitor and remedy.

Team 6: Membrane Transporters and Resistance (TMR)

Name of team leader: Ms Anne LESPINE

Workforce

Team workforce	Number as at 30/06/2014	Number as at 01/01/2016
N1: Permanent professors and similar positions	1	1
N2: Permanent EPST or EPIC researchers and similar positions	2	2
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other researchers (DREM, postdoctoral students, visitors, etc.)	1	1
N6: Other contractual staff (without research duties)	1	1
TOTAL N1 to N6	**6**	**6**

Team workforce	Number as at 30/06/2014	Number as at 01/01/2016
Doctoral students	2	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit	3	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	2

•Detailed assessments

Assessment of scientific quality and outputs

The research activity of the team is focused on the adaptations to drugs and xenobiotic interactions with mammalian and nematode models. They are in the line of two major axis of TOXALIM: “regulation of barrier function” and “pharmaco-toxicokinetics and bio-transformation”. Their past work has demonstrated a number of interesting interactions between the efficacy of anti-infective drugs and their affinity for ABC transporters. They focused on 1) anthelmintic macrocyclic lactones (MLs) whose resistance can develop in livestock, 2) ABCB1, which is the limiting factor in the access of MLs. For instance, they have shown that ivermectin impacts its own bioavailability through E- and T-MX regulation. Very interestingly, they also demonstrated that the mechanism does not involved directly one of the three xenobiotic receptors (AhR, PXR, CAR) and this clearly opens new forthcoming projects for the team. Moreover, they identified an alternative molecule to ivermectin (moxidectin, less toxic), which could be relevant for clinical purposes.

Since 2009, the scientific production of this small team (2 full-time researchers), is very good: 28 articles were published with a mean IF around 3,5 (28% in the first Quartile). The number of peer-reviewed publications with IF per N1 and N2 researchers is 9 over the last 5 years. As demonstrated by the list of publications involving internal or external collaborations (12 out of 28, 43%), the expertise of this team is widely recognized. The results of the team (16 out of 28, 57%) are published in excellent journals. Particularly, we retain excellent publications in scientific journals in the field (*Biochem Pharmacol*, IF 4,7; *Plos Neglect Trop Dis*, IF 4.9). In addition, the team deposed 1 international patent.

Short appreciation on this criterion

The scientific quality and outputs of the team are excellent due to their originality of their research in the pharmacolo-toxicological area and their scientific production regarding the size of the team (and the technical and administrative difficulties the members had to face (removal…)) and considering its diversity (articles, patent).

Assessment of the team's academic reputation and appeal

The visibility of the team (mainly due to the team leader) is high considering the pharmaco-toxicology area, in particular in response to anti-infective agents. One young scientist introduced the *Caenorhabditis elegans* model in the unit (HDR programmed in 2015) and should increase her visibility in the next few years.

The level of contribution to meetings is good (4 international communications, 7 national communications) although most invitations have mostly been to meetings in France (7 invitations).

The team (2 HDR between 2009-2014) appears to be very attractive for M2 (6), and attractive for PhD students (3). Its integration into TOXALIM is logical in regard of its two major research areas. In spite of the good scientific quality, there is no recruited post-doc.

The team has a significant activity in term of student training (6 Master 2, 3 PhD students from 2009-14). They are involved in teaching activities (1 MCU, teaching in 4 M2R, responsibility of lessons in Biochemistry and enzymology). They have 4 international collaborations (including a strong one with Pr R. Prichard). They have obtained an international patent in 2013 (ABCB1 inhibitor).

Short appreciation on this criterion

The team's academic reputation and appeal are excellent due to their high visibility worldwide, their dynamics (implementation of a new model) which should reinforce this visibility, the level of communication in regard to the numbers of PI. Their visibility is high in the toxicological field but also in universities at the national level considering the high number of trained students.

Assessment of the team's interaction with the social, economic and cultural environment

Economic environment: The research of the team is supported by ICSA (Institute Carnot Animal Health network), the metaprogram GISA and the EMIDA ERA-NET European network.

Social and cultural environment: The team members are highly involved in expertise (PhD, HDR juries, INSERM committees), scientific dissemination to the public and interaction with industrial partners.

Short appreciation on this criterion

The team's interaction with the social, economic and cultural environment are very good. The team is very well supported by national and international networks but also industrial partners. The members of the team are clearly involved in valorisation of their research and in various expertises.

Assessment of the team's involvement in training through research

The involvement of the team in training through research is very good. The team has trained 4 PhD students and 2 are in progress). In addition, 8 master-level students have been supervised (4 M1, 4 M2). Given the small number of qualified research supervisors with an HDR (2), it's very good. The involvement of the team members in teaching activities is huge mainly due to the activity of Ms Chantal LEBRUN (+20 h for the team leader).

Short appreciation on this criterion

The team's involvement in training through research is very good. Due to their high visibility and their very good production, the team is appealing for students. The originality of their work is also attractive. To reinforce this criterion, the team needs to increase its HDR number.

Assessment of the strategy and the five-year plan

The research project will focus on the fields of resistance to anti-infective agents. Three main axes will be developed:

1. Mechanisms of regulation of detoxification systems: this is logical in view of previous results, which are not explained by the involvement of nuclear receptors (PXR, CAR) or the AhR. Beside its fundamental interest, this might result in the identification of new targets for clinical purposes. Several models will be used for this important part.
2. Functional characterization and structural modelling of parasitic nematodes: this axis is complementary of the first one and then fully legitimate. It will bring an interesting link between structure and function of nematode xenobiotic metabolism transporters.
3. Search for strategies for optimization of MLs efficacy: the team aim to test associations to target nematodes. While probably interesting, very few details are present in the document (association of flavonoid-rich plants, MLs).

Short appreciation on this criterion

The strategy and the five-year plan are very good. Beside the frequent changes of the research projects, the new five-year plan developed by the whole team appears to be focused, ambitious (but not over-ambitious) and original. This should contribute to their high visibility and attractiveness.

Conclusion

This is a dynamic team (patent, development of new models, teaching, raising funds, international collaborations) with a very good visibility on the international “anti-infective agents” area and several original projects.

- Strengths and opportunities:

The main strengths of this dynamic team are:

- very Good expertise of the mechanism of action of the anti-infective agents with a transfer to biotechnologies (1 international patent);
- PhD students publish their results (3 PhD defences) Two original results in the field regarding the link between obesity and the deficit in one BC transporter and the interaction between food contaminants and ABC transporters (then a new model of knock-out mice);
- a young scientist has been recruited in 2010 (Ms Cécile MENEZ) and has developed C. *elegans* experiments for the team (but also use of Xenopus eggs models). This is a very important point for the future projects;
- excellent international visibility (patent, collaborations including a strong one with a Canadian team, Pr RICHARD; European networking);
- organization of small meetings and involvement in teaching (L and Master).

- Weaknesses and threats:

The main weaknesses of this team are:

- significant decrease of team size (compared to 2011);
- frequent changes of the research projects (interesting topics will disappear (obesity and KO mice)). A stabilization of the projects package is needed;
- few collaborative projects within TOXALIM;
- it is planned that the team will move from TOXALIM to the Vet School, which will significantly impact the activities of the team if not accomplished efficiently and properly supported.

- Recommendations:

The team has chosen to focus on the anti-infective agents which is a significant improvement compared to the former evaluation (with frequent changes of the projects). However, the size of the team is falling and this needs to be addressed, especially in view of the number of projects being undertaken, which, while interesting, might be too ambitious for the staff numbers available.

The recruitment of another member is probably be needed.

Another HDR laureate is necessary for 2015.

Team 7: Pharmacokinetics; pharmacodynamics and modelling

Name of team leader: Mr Alain BOUSQUET-MÉLOU

Workforce

Team workforce	Number as at 30/06/2014	Number as at 01/01/2016
N1: Permanent professors and similar positions	3	3
N2: Permanent EPST or EPIC researchers and similar positions	2	2
N3: Other permanent staff (without research duties)	2	2
N4: Other professors (PREM, ECC, etc.)	1	1
N5: Other researchers (DREM, Postdoctoral students, visitors, etc.)	1.5	
N6: Other contractual staff (without research duties)	2	1
TOTAL N1 to N6	**11.5**	**9**

Team workforce	Number as at 30/06/2014	Number as at 01/01/2016
Doctoral students	4	
Theses defended	6	
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	3	3

•Detailed assessments

Assessment of scientific quality and outputs

The team works on antibiotics and antimicrobial resistance, in order to promote prudent use of antibiotics in the food industry, and for veterinary or human drugs. The strength of the team lies in pharmacokinetic and pharmacodynamic modelling, and in the direct relevance of the subject for the veterinary and human medical field. The approach leads to publications in high-ranking journals, with high number of citations per paper and attracts collaborations with agencies and industry. The number of peer-reviewed publications with IF per N1 and N2 researchers is 15 over the last 5 years.

Short appreciation on this criterion

The scientific quality and outputs of the team are of good standing, particularly in the field of modelling. The competence of the team is multidisciplinary and has an established recognition in the scientific community.

Assessment of the team's academic reputation and appeal

Members of the team are regularly invited to speak at international conferences. The team has attracted 12 grants, 10 of which national, and participates in several networks, and has collaborations with several foreign research institutes.

Short appreciation on this criterion

The team has a very good reputation. The participation to international and national projects is good and the team is also involved in collaborative networks.

Assessment of the team's interaction with the social, economic and cultural environment

There is a good interaction with industrial partners as judged by the number of presentations, and seminars. There is ample links with research institutes and industry, and reports in technical and professional publications. A weak point is the low frequency of dissemination of knowledge to the general public, which is surprising concerning the resistance against antibiotics part. Also, exploitation of the results should be increased.

Short appreciation on this criterion

The very good interaction with industry should lead to more visible valorisation. Dissemination of knowledge to the general public as well as exploitation of the results should be improved.

Assessment of the team's involvement in training through research

The team has trained 7 PhD's, 2 post-docs, and 9 Masters students. Team's members have been involved in international teaching and they have responsibilities for master degrees with the co-direction of two master degrees and of the University diploma (DU) in Pharmacokinetics at the University of Toulouse.

Short appreciation on this criterion

The team's involvement in training through research is good. Team's members are involved in teaching at national and also at international level.

Assessment of the strategy and the five-year plan

A strong point of the team is the biostatistical modelling, and it intends to extend this in the coming years. Tools and collaborations are present to assure success in this area. The other axis is the one on antimicrobial resistance, which requires data, and hence experiments and expertise to obtain it. Plans are to further develop the experimental models such as the biofilm system, and the team themselves questions whether the bacterial metagenomics skills should developed within the team (requiring investment) or obtained through collaborations. We feel that the data generation is new for the team, would require too much investment before sufficient expertise is acquired. The team should instead consider expanding their network to obtain these data, and should also extend their cooperation with other teams within TOXALIM for that purpose.

Short appreciation on this criterion

The team should focus on their core expertise biostatistics, in which they are very good. The development of collaborative networks is recommended to fill the lack of expertise in metagenomics.

Conclusion

The team presents multidisciplinary competence and has an established recognition in the scientific community. It is recommended that the team focus future strategic plans upon bioinformatics approaches, the team having already expertise in mathematics, biostatistics and modelling.

- Strengths and opportunities:

The team is strong in biostatistics and its applications. It also has a good network to attract funding in that area. Both are a good basis for competing in high dimensional data analysis.

- Weaknesses and threats:

The presence of a second objective (data generation itself) may weaken the focus and the core expertise.

- Recommendations:

The team should rethink their strategy to focus upon bioinformatics approaches.

Team 8: Genotoxicity and Signalling (GS)

Name of team leader: Ms Gladys MIREY

Workforce

Team workforce E8 GS	Number as at 30/06/2014	Number as at 01/01/2016
N1: Permanent professors and similar positions	3	3
N2: Permanent EPST or EPIC researchers and similar positions	1	1
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other researchers (DREM, postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)	1	2
TOTAL N1 to N6	**6**	**7**

Team workforce E8 GS	Number as at 30/06/2014	Number as at 01/01/2016
Doctoral students	3.5	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	2	3

•Detailed assessments

Assessment of scientific quality and outputs

The research of this team is very well balanced between fundamental and applied research in the field of genotoxicity of environmental contaminants.

Two aspects are specifically addressed by this team: 1. DNA repair mechanisms; 2. Genotoxicity of biological and chemical agents. Members of this team (formerly belonging to the CNRS team “Radiobiology and DNA repair”) have significantly contributed to the understanding of the mechanisms of double-strand breaks (DSB) repair by end-joining mechanisms. Some of this excellent research has been taken on board by this new team that emerged in 2011 (with 4 members from the CNRS team) producing publications in highly ranked journals. The research activity on the genotoxicity of biological and chemical agents has produced interesting results (e.g. development of new genotoxicity assays, identification of the mechanism of action of bacterial genotoxins) but the publication rate on these topics suffers of the very recent investment in this area of this group. A significant number of the team publications (18) has

been published in highly ranked journals (average IF 7) although the large majority (14) involve several researchers of the CNRS Team. The publications in collaboration (12) are more heterogeneous in terms of subject area but still are characterized by high IF journals. The ratio of peer reviewed publications with IF per N1 and N2 researcher over the last 5 years is 7.

This team is involved in several national collaborative networks but should improve the international collaborations.

Short appreciation on this criterion

This team is scientifically very active and the high level of fundamental research shows a continuum with the excellence of CNRS team from which some of the members derive. The publication rate and quality in DNA repair mechanisms is excellent but when considering the all production (including that related to the most applied research activity) it can be considered very good only.

Assessment of the team's academic reputation and appeal

The leadership in national programs is relevant (7 projects as coordinators) while is limited in international projects (3 as partners). However, the unfortunate limited visibility of the research topics of this unit within the currently granted EU research projects at least partially accounts for this apparent weakness. Conversely, the academic activity of this team is significant (almost all team members involved in teaching). This activity should be more balanced with research activity considering also the small size of this unit.

The ability to raise funding is very good at the national level (8 grants, 5/8 as coordinators), 2 regional grants, and 5 INRA/University grants. No grants at international level.

The visibility as invited speakers at international conferences is limited (5) but higher at national level (9). The same applies to oral communications mostly at national meetings (9/15). The improvement in the development of international collaborations would help from the perspective of international visibility.

The team publishes in highly ranked journals (e.g. Oncogene, Nucleic Acids Res., EMBO J).

Short appreciation on this criterion

The team's academic reputation and appeal are overall good. The group should be encouraged to gain higher international visibility through participation to international projects/meetings. The main contribution of the team to training and education is recognized, however, this small team would benefit of a better balance between teaching and research activity.

Assessment of the team's interaction with the social, economic and cultural environment

The knowledge dissemination is covered by the participation in several national/international meetings and through the participation of some of the members to scientific committees of national and international public health bodies.

This team developed an interesting technique, i.e. nanobodies, which resulted in one international patent.

There is a good investment of the team in external communication with many conferences and seminars that however involve almost solely one member.

Short appreciation on this criterion

This is a small team that should to be supported by stimulating internal and external collaborations. The international collaborations and visibility should be improved. In summary, team's interaction with the social, economic and cultural environment is very good.

Assessment of the team's involvement in training through research

The teaching activity heavily involves most of the team members (about 200 h/year) with three members having also responsibility of teaching units. Team’s members are involved in master’s training programmes (2

members) and PhD colleges (1 member). During the last 5 years the team's members supervised one visiting PhD, 5 Master1 e and 9 Master2 students and participated to 3 HDR and 12 PhD jurys.

Short appreciation on this criterion

The team is significantly involved in training and education. Its involvement in training through research is thus very good. However, considering the size of the team, there is an unbalance towards teaching more than towards research, which should be corrected.

Assessment of the strategy and the five-year plan

The 5-year plan consists of research activity within a large epidemiological study on the risk of exposure to pesticides. The study will use classical biomarkers of effect/susceptibility study and more mechanistic studies on the genotoxicity of emerging risks (i.e. bacterial genotoxins and nanoparticles). The proposals are scientifically sound but particularly the large project on the effects of pesticides misses a more updated approach to the evaluation of risks for human health of environmental contaminants. The application of "omics" (untargeted approach) is strongly recommended within an exposome-like experimental design. The use of innovative cell models for the analysis of the genotoxic effects of food-born contaminants is of interest and will produce relevant information by taking into account the issue of cell/tissue target specificity in DNA damage response. The development of innovative tools for genotoxicity assessment is important and addresses a need in the field of screening of chemicals and identification of biomarkers of exposure/effect. The 5-year plan is feasible. The SWOT analysis tackles all relevant points.

Short appreciation on this criterion

The 5-year plan is pertinent and based on the expertise of the team. The innovative aspects should be supported. Efforts are required to apply more innovative strategy in human biomonitoring studies. In summary, the strategy and the five-year plan are very good.

Conclusion

The fundamental research in DNA repair is a major strength of this team and should be continued also as relevant source of innovative tools for more applied research (see identification of new pharmacological targets; development of new genotoxicity assessment tools). The approach to biomonitoring studies should be revisited with a more modern and innovative strategic approach.

- Strengths and opportunities:

The main strengths of this team are a high level of publications in DNA repair fundamental research and development of innovative tools for HTS and pharmacological targeting.

- Weaknesses and threats:

The main weaknesses of this team are its small size with researchers also deeply involved in teaching and also the fact that the applied research misses international dimension.

- Recommendations:

The committee has the following recommendations for this team:

- strengthen the research dimension of the team by recruitment of a technical/full-time researcher;
- improve the collaboration with other teams/platforms using "omics" approaches;
- investigate the possibility of negotiating a reduction in teaching load.

Team 9: Prevention and Promotion of Carcinogenesis by Food (PPCA)

Name of team leader: Ms Françoise GUÉRAUD

Workforce

Team workforce	Number as at 30/06/2014	Number as at 01/01/2016
N1: Permanent professors and similar positions	2	1
N2: Permanent EPST or EPIC researchers and similar positions	4	4
N3: Other permanent staff (without research duties)	3	2
N4: Other professors (PREM, ECC, etc.)		
N5: Other researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**9**	**7**

Team workforce	Number as at 30/06/2014	Number as at 01/01/2016
Doctoral students	3	
Theses defended	3	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	3	3

•Detailed assessments

Assessment of scientific quality and outputs

This team is proposed in the context of renewal of "TOXALIM". It was already present in the former "TOXALIM" but the leader is now changing (Ms Françoise GUÉRAUD for the next 5 years, Mr Denis CORPET PREX from 2009-2014).

The team analyses the mechanical link between consumption of red meat and colorectal cancer. They are now in the line of several axis of TOXALIM and develop collaborations with 3 teams (4, 8, 11). Their past work has demonstrated that processed red meat promotes CRC and the role of heme iron in this carcinogenic process. In addition, they have demonstrated a unique feature of CRC cells regarding dietary lipid oxidation products and the contribution of Nrf2-dependant mechanisms in those processes. They also focused on the development of preventive actions to inhibit the carcinogenic effects of heme. Calcium or vitamins are key factors in their work (food interactions), which has been also translated in humans (to quantify the production of carcinogenic products after consumption of red meat (ex: +/- calcium or tocophérol)).

Number of publications during 2009-2014: 44 publications (22 original articles from the group; 22 other pub), 7 book chapters, 14 international and 7 national oral communications. The ratio of peer reviewed publications with IF per N1 and N2 researcher over the last 5 years is 7. Several journals are in a very good range of impact factors regarding "toxicology and nutrition".

Short appreciation on this criterion

In summary, the scientific quality and outputs of the team are very good due to their dynamics, their production and the various expertises developed on the bench. As a consequence, their national and international visibilities are very high. The new team leader is highly legitimated regarding its expertise and position in the team.

Assessment of the team's academic reputation and appeal

The visibility of the team is high considering the "nutrition/toxicology" area, with a lot of invitations to international meetings.

The team (2 HDR between 2009-2014) appears to be very attractive for PhD students (3 + 3). In spite of the good scientific quality, there is no post-doctoral scientist on the team (this is a choice; the team mainly focus on the training of PhD students).

Several members of the team have been invited to international (13) and national (8) conferences. Their research has been highlighted in mainstream media (the Wall Street Journal).

In summary, the team has a significant activity in term of:

- student training (3 PhD students from 2009-14, 3 for the next periods);
- they coordinate 3 ANR (1 Blanc international), 1 INCA, 2 Ligue and 1 industrial projects;
- some team members belong to editorial boards or expert bodies (ANSES, INCA);
- they have a high number of international and national collaborations.

Short appreciation on this criterion

The team's academic reputation and appeal are excellent due to their huge visibility worldwide (media, conferences…). The team shares its expertise for agencies, developed collaboration with the academic world and industrial partners and is able to attract a significant number of students.

Assessment of the team's interaction with the social, economic and cultural environment

The link with industry is very high. Many seminars and conferences have been presented to the general public by the former team leader. Again, their research has been highlighted in mainstream media (including the Wall Street Journal). On this criterion, the team is one of the most dynamic of ToxAlim and should help to reinforce it for other teams.

Short appreciation on this criterion

The team's interactions with the social, economic and cultural environment are excellent. The team is very well supported by academic and industrial partners. The team is also very dynamic to disseminate their work. The change of team leader should not (and must not) change this criterion.

Assessment of the team's involvement in training through research

The involvement of the team in training through research is very good. The team has trained 6 PhD students (3 are in progress). In addition, 5 master-level students have been supervised (1 M1, 4 M2). Given the number of qualified research supervisors with an HDR (3) it's very good. The involvement in teaching is quite low but is compensated by the valorisation of their work for the general public.

Short appreciation on this criterion

The team's involvement in training through research is very good. Due to their high visibility and their very good production, the team is quite appealing for students. The high valorisation of their work is also probably very attractive.

Assessment of the strategy and the five-year plan

Inside TOXALIM, the team is composed of 3 CR1 (team leader HDR), 1 DR2, 1 IE1, 1 TREX, 1 MCHC, 1 IR2 & 3 PhD. The research project is in the line of the results but is built to improve the technical expertise of the team (development of new models and methods). The team:

- will characterize the effect of HNE (4-hydroxyneonenal) *in vivo*;
- aims to develop new methods to study the role of FeNO in CRC development *in vivo* (encapsulation) and new models (*in vitro* model of human colon cancer cells);
- will study new food interactions will be studied (fatty acid context);
- will analyse the role of Nrf2 in several original process with the IRSET and INSERM 966;
- will continue to find new preventive methods (protective compounds delivered to the gut by encapsulation).

The team has all the expertise required to lead those projects even if their number appear to be very high relative to the number of team members.

Short appreciation on this criterion

The strategy and the five-year plan are very good. The projects are in the line of their former research. The new five-year plan developped by the whole team is still very focused and ambitious. This should contribute to maintain their high visibility and attractiveness.

Conclusion

This is a very dynamic team in research and exploitation of their research (including expertise activities) with an excellent international visibility.

- Strengths and opportunities:

The main strengths of this team are:

- a balanced team with complementary expertise;
- excellent expertise of the link between red meat and CRC (at the mechanical level);
- the team is well financed;
- international visibility is high (invitations, ANR and international, collaborations);
- strong interaction with industry to improve processed red meat;
- PhD students publish their results (3 successful PhD defences);
- lots of collaboration inside TOXALIM;
- organisation of a small meeting.

- Weaknesses and threats:

The main weaknesses of this team are:

- low involvement in teaching;
- focus on colon epithelial cells, not the whole environment;

- Size of the projects.

  - Recommendations:

Regarding the size of the project, the recruitment of another ITA member might be needed.

The development of a new *in vitro* model should be a focus.

Team 10: Xeniobiotic's Cellular and Molecular Toxicology (CMTX)

Name of team leader: Mr Roger RAHMANI

Workforce

Team workforce E10-TCMX	Number as at 30/06/2014	Number as at 01/01/2016
N1: Permanent professors and similar positions	1	
N2: Permanent EPST or EPIC researchers and similar positions	3	3
N3: Other permanent staff (without research duties)	2	3
N4: Other professors (PREM, ECC, etc.)		
N5: Other researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**6**	**6**

Team workforce	Number as at 30/06/2014	Number as at 01/01/2016
Doctoral students	1	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	2	2

•Detailed assessments

Assessment of scientific quality and outputs

The team concentrates on toxicant mixtures and the cellular and molecular pathways involved in translating exposure into adverse outcomes.

In terms of national and international conferences, 6 invited talks and 31 talks and posters were presented by the team. The team has averaged 7 publications with IF per N1+N2 staff over the last 5 years, reflecting 31 peer-reviewed publications, 20 by the team alone and 11 in collaboration with other TOXALIM teams (1.4 publications per permanent position per annum). These publications averaged a 5-year impact factor of 3.2. Given the nature of the work the team performs, it was surprising that their highest impact factor journal was 5.5 and it was also not evident what share of the publications involved international collaborations. This output is good but not outstanding although the presence of team members as first and/or senior authors suggests that a lot of the work is internally generated by the team, which makes the output more impressive.

Short appreciation on this criterion

The scientific quality and outputs are very good. Although the average IF of the publication of this team is not impressive, it should be considered that the work is mostly generated internally by the team. The balance between output and IF is hampered by the relatively low Ifs of most of the appropriate journals, a factor beyond the control of the team. However, the quality of the work performed suggests that this team could be more ambitious in terms of trying higher impact journals with their best work.

Assessment of the team's academic reputation and appeal

The clearest signs of recognition are invitations to participate in conferences and collaborative projects. The team are involved in a number of local and national networks and collaborations (7 of the latter) but appear to have only a single international collaboration. Only 1 team member notes international journal editorial board membership and unfortunately the journal is discontinued. The team does however provide expertise to 6 national and international public bodies (e.g. AFFSET). The team had 12 invitations to national and international conferences/seminars over the 4 years, with 2 poster awards given to team members.

As far as the committee can judge, the team did not participate in international funding during the reporting period. They did however participate in 8 national projects and coordinated 2 of them. Unfortunately, the amounts raised were not indicated which hampers assessment since two very large grants would be far more important than several much smaller grants. That said, 8 national grants in 4 years, especially if they are of reasonable size, is a good performance.

Short appreciation on this criterion

The team's academic reputation and appeal are very good based on invitations as main speakers in conferences and on collaborations. However, international collaborations should be improved as well as participations in international grants. The bulk of the invited presentations are given by the team leader indicating a good profile in the field. Other members of the team are invited and acting to give presentations. The list of collaborations is quite modest but is diverse, indicating good appeal within the field of research.

Assessment of the team's interaction with the social, economic and cultural environment

In terms of direct industrial links, the team has very modest connections, consisting more of presentations to industrial audiences but they were instrumental in the NEOMAH Research in Toxicology start-up (contributing to a patent also), which looks like it has the potential for considerable impact. The team has concentrated of scientific communication and present little evidence of communication with the public. However, and importantly, they have contributed to a number of expert committees and government (e.g. ANSES and presentations to the Senate, National Assembly and government ministries). This would be rated “very good”.

Short appreciation on this criterion

The team's interaction with the social, economic and cultural environment is good. This conclusion is based on their good participation in industrial and technical institutions as well as their involvement with safety agencies and working groups. Finally the group shows good levels of participation with both national and international public bodies.

Assessment of the team's involvement in training through research

The team has trained 4 PhD students (3 apparently successfully defended), 4 post-doctoral scientists, 5 masters students, 2 foreign students, 2 thesis in medicine students and 3 scientists to successful HDR defence during the reporting period. Given that 2 staff members have their HDRs this can be considered an excellent (top 20% effort) effort. In terms of other teaching, the team contributes 22 hours/year, which is quite modest. This may represent some missed opportunities to come into contact with students who would be in future cohorts of MSc and PhD candidates.

Short appreciation on this criterion

The number of PhD and master students shows a considerable effort in training but the time devoted to didactic/undergraduate teaching (as opposed to training) of team's members is modest. Overall the team's involvement in training through research is very good. This rating is given because with only 2 HDR staff, training 20 scientists, 5 per annum, ranging from masters to PhD and HDR represents a strong effort. Furthermore, since the team does only modest teaching, they are still managing to attract project, masters and PhD students without prolonged exposure to a cohort of undergraduates as potential laboratory recruits.

Assessment of the strategy and the five-year plan

The master strategy for the 5 year plan is closely based on (i) the team's track record and (ii) research, testing and regulatory challenges of toxicant mixtures. In my view 2.1 is the most exciting and relevant component of the plan, 2.2 is more focused on the detailed biomolecular and genetic pathways and mechanisms of action of a selected POP, chloredecone. This component is likely to deliver important and translatable data but deviates from the mixture approach of 2.1. Section 2.1 of the plan suggests considerable potential and if successful in its parts, such as the Horizon 2020 application EUROMIX and the national METABOMIX, should enable the team to have critical involvement in internationally-relevant studies of toxicant mixtures. The combination of animal and *in-vitro*/*in-silico* approaches should enable the team to also increase their impact. Given the UN's recent declaration for a move away from industrial to organic farming, 2.1.1 is highly timely. The research and output over the past reporting period suggests that the team will be able to perform the work to a sufficient standard.

Short appreciation on this criterion

The strategy and the five-year plan are excellent. This rating is based on flexibility and innovation of the team's forward thinking. Specifically, the proposed program squarely addresses the new challenges in toxicology by proposing a shift from traditional animal-based toxicology to *in vitro* and *in silico* approaches based on human material. Their emphasis on mixtures of toxicants and the combination of approaches is excellent. It is likely that the team will produce important new advances from the 5 year plan. This was reinforced by the presentation and discussion afterwards, together with the team news highlighted below.

Conclusion

The small CMTX team has a respectable research profile and output and demonstrate good focus. Their achievement and interaction with relevant national agencies and government is strong. The research programme is sufficiently cohesive and coordinated to make good progress in the field and to achieve international relevance. The team does, however, need to raise its ambition levels a little since there is the sense that they could do even better in the next 5 years. It is likely that achieving the Horizon 2020 funding "EUROMIX" would help them do so.

- Strengths and opportunities:

The main strengths of this team are:

- the team has the necessary skills and expertise;
- team leader seems to lead from the front by example;
- credible and sufficiently focussed research programme;
- very good production of completed PhD students;
- very good and achievable 5 year plan (subject to funding success).

- Weaknesses and threats:

The main weaknesses of this team are:

- limited international collaboration and publication;
- no international grants (NB see below);
- limited teaching activities;

- medium level impact in terms of publications;
- limited public communication.

- Recommendations:

The team appears to have good cohesion and probably about the right level of collaboration nationally. However, the team should increase its international presence somewhat with more relevant international collaboration/grants and perhaps a bit more ambition in terms of seniority of journals used for publication of team findings.

However, it must be noted that at the evaluation it transpired that CMTX had been successful in obtaining Horizon 2020 funding (EUROMIX). They are to be congratulated on addressing their main weakness even before receiving this report.

Team 11: Intestinal Development, Xenobiotics and Immunotoxicology (DIXIT)

Name of team leader:

Mr Éric HOUDEAU

Workforce

Team workforce E11 DIXIT	Number as at 30/06/2014	Number as at 01/01/2016
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	2	2
N3: Other permanent staff (without research duties)	2	2
N4: Other professors (PREM, ECC, etc.)		
N5: Other researchers (DREM, postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**4**	**4**

Team workforce E11 DIXIT	Number as at 30/06/2014	Number as at 01/01/2016
Doctoral students	0.5	
Theses defended		
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	2	2

•Detailed assessments

Assessment of scientific quality and outputs

Team 11 started its activity in November 2013. Before that date, the researchers worked in teams 4 and 5. Accordingly, the scientific report for that (2009-2014) is in common to those teams.

The team presents a scientific report with 21 publications authored by the two permanent positions (N2) of the team: Mr Éric HOUDEAU and Ms Laurence GUZYLACK-PIRIOU. Therefore, the mean number of articles published/permanent positions is 10.5 over the last 5 years.

Since November 2013, the research topics of the team deal with the sensitivity of the intestine when exposed to xenobiotics like endocrine disruptors (bisphenol A) and nanoparticles, which can be present in the diet. The toxic

effect of these substances is studied in adults but also in the perinatal period. Actually, the attention is focused on the toxicity during specific (perinatal) periods of development of the immune system in the gut, which according to the researchers can have negative consequences also in the adult life of the individual.

Short appreciation on this criterion

The scientific production in the past years has been excellent (24 papers, the major part as Q1). Most of the publications are in journals with high impact factor and have a very good citation index. In summary, the scientific quality of the team seems excellent.

Assessment of the team's academic reputation and appeal

The team is partner in a consortium of various French labs addressing nanomaterials toxicity (Labex SERENADE).

One researcher of the team (who is also representative for AlimH Division) belongs to a National network for the study of the toxicology of nanoparticles.

Coordinator of four research projects in Food Toxicology focused on nanoparticles and endocrine disruptors (no mention of the amount of the funding).

The team has organised a National joint meeting with the ANSES ("Agence Nationale de Sécurite Alimentaire").

Short appreciation on this criterion:

The team is partner in a French consortium on nanomaterial toxicity (Labex SERENADE). They are involved (as coordinator) in Food Toxicology projects on nanoparticles and endocrine disruptors and organised a National joint meeting with the ANSES ("Agence Nationale de Sécurite Alimentaire"). Moreover the team published in in journals with high impact factor and these papers have a very good citation index. In conclusion, the team's academic reputation and appeal is very good

Assessment of the team's interaction with the social, economic and cultural environment

As reported above, two publications by the team have been opened to a press release (those dealing with the effects of low doses of BPA during the perinatal period, reference #1 and #8 in the list).

Members of the team have been invited to give 5 seminars and conferences (not specified where). The also gave interviews in magazines/radio/TV). They participated to a national agricultural convention.

Short appreciation on this criterion:

Two publications by the team have been opened to a press release; members of the team have been invited in scientific conferences as well to give interviews in magazines/radio/TV. They also participated to a national agricultural convention. Therefore, the interaction of the team with the environment is excellent

Assessment of the team's involvement in training through research

Since 2009, the team trained 5 PhD students and 1 post-doc. It obtained 2 grants through the Labex SERENADE (nanoparticles research) and INRA/Region for new PhD positions. Teaching activity is limited.

Short appreciation on this criterion:

The team trained PhD students and one post-doc. Two new PhD positions, granted by Labex SERENADE, have also been obtained. In summary, the team's involvement in training through research is very good

Assessment of the strategy and the five-year plan

Projects for the next five years deals on the sensitivity of the intestine to oral exposure to different classes of food contaminants (BPA-like substances and nanoparticles); these topics are coherent with the field of research

proper of the team. The researchers will also carry out basic research related to the hormonal control on epithelial and immune functions of the gut as related to gender, and different periods of the life (perinatal, puberty etc.). According to the report, various grants have been obtained on these topics, and many collaborations are in course. The two PhD students are funded by such grants.

The research on the toxicity of various derivatives of bisphenol A (BPA), is a continuation of their previous studies on the toxicity of BPA, which will be banned in France. These possible substitutes, already present in some costumer products, also raise concern, so it is important to make research on them. Interestingly, the research will also evaluate mechanism of action underlying this toxicity studying the involvement of the Ah and ER receptors and the interplay with the microbiota. Various experimental models will be used, also in collaboration with other TOXALIM units. The other part of the five year project will be on nanoparticles (NP), in particular the fate and the effect of food-grade nanomaterials after oral exposure. They will use experimental models *in vitro* (human buccal epithelial cells) and *in vivo* (pigs) in collaboration with other units of TOXALIM (not specified which). Based on preliminary data indicating that NP accumulate in Peyer's patches, they will investigate how NP may affect intestinal barrier function and the gut immune system.

Given the expertise and the facilities of the team the projects are perfectly feasible.

Short appreciation on this criterion

The strategy and the five-year plan of the team are excellent. Given the expertise and the facilities available, the proposed research is perfectly feasible.

Conclusion

This is a small team with a strong involvement in research in topics very relevant for food toxicology.

Strengths and opportunities:

The main strengths of this team are:

- the team is small but with a strong involvement in research activity;
- various collaborations;
- the topics are very relevant.

Weaknesses and threats:

The main weakness of this team is its small size.

Recommendations:

Given the small size of the team and the many research topics, additional researcher(s) should be recruited.

Team 12: Plateforms AXIOM-EZOP-M2C and TRIX

Name of team leader: Mr Bernard SALLES

Workforce

Team workforce (in FTEs)	Number as at 30/06/2014	Number as at 01/01/2016
N1: Permanent professors and similar positions		1
N2: Permanent researchers from Institutions and similar positions	12	11
N3: Other permanent staff (without research duties)	14	18
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)		
N5: Other researchers (Emeritus Research Director, Postdoctoral students, visitors, etc.)		4
N6: Other contractual staff (without research duties)	2	4
TOTAL N1 to N6	**28**	**38**

The plateforms were not evaluated.

Team 13: Common services

Name of team leader: Mr Bernard SALLES

Workforce

Team workforce (in FTEs)	Number as at 30/06/2014	Number as at 01/01/2016
N1: Permanent professors and similar positions	1	1
N2: Permanent researchers from Institutions and similar positions	1	1
N3: Other permanent staff (without research duties)	12	11
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)		
N5: Other researchers (Emeritus Research Director, Postdoctoral students, visitors, etc.)		2
N6: Other contractual staff (without research duties)	1	2
TOTAL N1 to N6	**15**	**17**

The common services were not evaluated.

5 • Conduct of the visit

Visit dates

Start: "Wednesday, 3, December, 2014", at "8:00"

End: "Thursday, 4, December, 2014", at "19:00"

Visit site: TOXALIM

Institution: UPS Toulouse 3, ENVT, Engineers School of Purpan and INRA

Address: 180 chemin de Tournefeuille, BP 93173, 31027 TOULOUSE CEDEX 3

Conduct or programme of the visit:

Day one – Date: Wednesday December 3	
08:00	Welcome (closed-door) Visiting committee with the HCERES Scientific advisor
08:15	HCERES **representative**: the role and procedures of HCERES
08:30	**Director of the unit: p**resentation of the unit and of its past activities
10:00	**Team 1 – Integrative Toxicology and metabolism (TIM)** *Name of the team leader: Mr Hervé GUILLOU*
10:50	**Team 4 - Neuro-Gastroenterology & Nutrition (NGN)** *Name of the team leader: Ms Vassilia THÉODOROU*
11:40	**Project of Team 11 - Intestinal development, xenobiotics and immuno-toxicology (DIXIT)**. *Name of the team leader: Mr Éric HOUDEAU*
12:15	**Team 5 – Biosynthesis and toxicity of mycotoxins (BTM)** *Name of the team leader: Ms Isabelle OSWALD*
14:15	**Team 9 - Prevention and Promotion of Carcinogenesis by Food (PPCA)** *Name of the team leader: Ms Françoise GUÉRAUD*
15:05	**Team 8 - Genotoxicity and signaling (GS)** *Name of the team leader: Ms Gladys MIREY*
15:55	**Team 2 - Metabolism of Xenobiotics (MeX)** *Name of the team leader: Mr Daniel ZALKO*
17:15	**Team 3 – Gestation and endocrine disruptors (GED)** *Name of the team leader: Ms Catherine VIGUIÉ*
18:05	**Team 10 – Cellular and molecular toxicology of xenobiotics (CTMX)** *Name of the team leader: Mr Roger RAHMANI*

Day two – Date: Thursday December 4	
8:00	**Team 7 - Pharmacokinetics, Pharmacodynamics and Modelling (PPM)** *Name of the team leader: Mr Alain BOUQUET-MELOU*
8:50	**Team 6 - Membrane Transporters and Resistance (TMR)** *Name of the team leader: Ms Anne LESPINE*
9:40	**Presentation of the project** *Mr Bernard SALLES and Ms Isabelle OSWALD*

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10:40	**Presentation of the platforms** AXIOM (Mr Laurent DEBRAUWER) TRIX (Mr Pascal MARTIN) M2C (Mr Thierry GAUTHIER) EZOP (Ms Elisabeth JEUNESSE)		
11:00	**Meetings with personnel:**		
11:00-11:30	Discussions with engineers, technicians, administrative	11:00-11:30	Discussions with students and post-docs
11:30-12:00	Discussions with staff scientists	11:30-12:00	Meeting with the director of the local doctoral school
12:00	**Discussion with the team leaders**		
14:15	**Discussion with the representatives of the managing bodies and partners**		
14:45	**Discussion with the head of the unit**		
15:15	**Private meeting of the visiting committee (in presence of the HCERES scientific advisor)**		

6 • Supervising bodies' general comments

The director of the unit does not wish to make any comments on this evaluation report.