



Istituto Superiore di Sanità

RESEARCH COLLABORATION AGREEMENT
for the implementation of the activities
"Virus dell'epatite E nelle carni suine
fresche e conservate"
[Hepatitis E virus in fresh and cured pork meat]

n. 2552

between

Istituto Superiore di Sanità, hereinafter referred to as "ISS" tax code 80211730587 based in Rome, Viale Regina Elena 299, post code 00161 represented for the drafting of the present Act by the Director of Human and Economic resources, Dr.ssa Rosa Maria Martoccia

And

Bundesinstitut für Risikobewertung, hereinafter referred to as "BfR", tax code DE165893448 based in Berlin, [Max-Dohrn-Str. 8-10], [10589], represented by its president Professor Dr. Dr. Andreas Hensel for the drafting of this Act by the Legal representative, head of the department Administration Michael Gose.

GIVEN THAT:

- The Italian Ministry of Health – Direzione generale per l'igiene e la sicurezza degli alimenti [General Directorate for Hygiene and Food Safety] deals with the hygiene and the safety of the production and commercialization of foods, the National Integrated Control Plan, the control plans of food chain, and in the coordination of laboratories involved in food control;
- The Italian Ministry of Health – Direzione generale per l'igiene e la sicurezza degli alimenti coordinates the national prevention plan 2014-2018, that includes actions for the implementation of the National Integrated Control Plan for food safety and veterinary public health;



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- ISS, as a part of its institutional mandate, provides scientific support to preparedness activities and response to emerging issues;
- ISS has signed a collaboration agreement with the Italian Ministry of Health for the realization of a project entitled "Virus dell'Epatite E nelle carni fresche e conservate [Hepatitis E viruses in fresh and cured meat]" starting on 27/09/2017 and closing on 26/09/2018;
- In the operational plan related to the above described activities and attached to the cooperation agreement with the Italian Ministry of Health are forecasted collaborations with BfR;
- With reference to the preamble, according with Art.15 of Law n.241 of 7th August 1990 and subsequent amendments and integrations, is in the intent of the parties to subscribe an agreement that governs the main terms of the collaboration in the specific project

IT IS AGREED AND STIPULATED AS FOLLOWS:

Article 1 (Subject)

The subject of this agreement is the collaboration between the ISS and the BfR that, within their respective competences and taking care about the objectives, agree to put in place jointly all the necessary actions for the realization of the project "Virus dell'epatite E nelle carni suine fresche e conservate", as stated in the Executive Project which is an integral part of this Act (Annex "A").

Article 2 (Duration)

The activities regulated by this Act shall take effect from 27/09/2017, starting date of the project and expiry on 26/09/2018.

The effectiveness of this Act is however subjected to its publication on the institutional ISS website regulated by Art.26, Decree n.33 of 14th March 2013.

Article 3 (Contribution)



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The funds allocated for the implementation of activities related to the project are Euro 18.000,00 (eighteen thousand/00) and will be transferred subject to the reception of the accruals from the Italian Ministry of Health to the ISS, that has the assignment of the expenses management for the full amount. The methods of transmission of funds will be as follows:

- 30%, equal to Euro 5.400,00 (five thousand four hundred /00) as advance payment, after the sign of this agreement and upon presentation of related payment request;
- 40%, equal to Euro 7.200,00 (seven thousand two hundred /00) after two months from the signature of this Agreement, following the reception by ISS of the scientific report of activities and of the intermediate financial statement referred to in art. 5 of this Act, and under presentation of the payment request;
- 30%, equal to 5.400,00 (five thousand four hundred /00) as final balance.

At the time of the balance liquidation, within 30 days from the expiry date of the present agreement, the BfR has to give ISS the following documentation:

- final scientific report of the activities carried out during the whole project;
- final analytical list of costs incurred according to the categories of costs resulting from the attached business plan together with a declaration signed by the legal representative drafted according to the attached fac-simile.

The payment requests related to the second tranche and to the balance will be issued only after notification by the ISS of the realized transfer of funds from the Italian Ministry of Health.

The transfer, being contribution nature, is out of the scope of Value Added Tax (VAT), according to Art. 4 of P.R.Decree 26/1/72 n. 633.

The BfR declares to be aware that the provision of the accruals of contribution will be done after the acquisition by the ISS according with the different funding rates by the Italian Ministry of Health, and undertakes to keep free the ISS from any possible claim from third parties concerning BfR`s contribution to the project.



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Article 4
(Scientific Manager)

The Scientific Managers employed to carry out the research activities will be for the ISS Dr. Dario De Medici and for the BfR Dr. Reimar Johné.

Article 5
(Accounts and Scientific Reports)

Within two months from the signature of this Agreement, BfR will send to ISS a financial statement showing the amounts committed and/or costs incurred.

Within thirty days after the expiry date of the agreement, the BfR communicates to the ISS a final technical report on the results achieved over the duration of the agreement and a final financial statement of the costs incurred for the realization of the project.

The reports referred to the preceding article shall be drafted by the BfR using the attached reporting template.

All the supporting documentation for the expenditures must be kept as record by the BfR that is committed to produce the originals or certified true copies of these documents under request of ISS within ten days of the same request.

ISS can ask at any time to know the progress status of the project.

The financial reporting of the preceding paragraphs shall be drafted according to the expenses items listed in the financial plans foreseen in the original project as "Reimbursement of BfR expenses" for the activities reported in annex A.

Article 6
(Management rules)

The contribution must be used exclusively for expenses related to the duration of the validity of this Act and in any case strictly concerning the realization of the research.

Any unused contribution share resulting from the submitted financial reporting must be sent back to ISS.



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Using funds for the rent/buy of local buildings, for the purchase of cars or for expenditures on various types of utilities (e.g. gas, electricity, etc) is not allowed.

The purchase of equipment is exceptionally allowed only when their use is directly linked to the implementation of the project and in any case after an evaluation of the cost-effectiveness in comparison with other forms of acquisition of the asset (rental, leasing). It is understood that it will be recognized the equipment depreciation rates, within the duration of the agreement and under presentation of the documentation.

Within the personnel expenses it is possible include all types of fixed-term employment contract provided by the law.

It is understood that, both in case of acquisition of external personnel and in case of using internal staff, the correctness of the recruitment procedures must always be verified by the executor entity according to the current legislation.

Article 7

(Publications and research results)

The results of the project, including the reports referred to in Article 5, are exclusive property of the Italian Ministry of Health. The rights of the property and/or the utilization and economic exploitation of the source files and original products, project documents, final technical report, intellectual property, intellectual creations, software procedures and other educational material, invented, designed or made within the cooperation activities between ISS and BfR detailed in point 3 of Annex A of this Agreement shall remain the exclusive property of the Italian Ministry of Health. The Italian Ministry of Health can dispose without any restrictions of the publication, broadcast, use, sale, transfer or partial assignment of such original works or materials, indicating those who were committed in their production. Pre-existing Intellectual properties, rights on material, know-how and procedures pre-existing this Agreement will remain exclusive property of the contributing part.



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Without prior authorization from the Italian Ministry of Health, both during and after conclusion of the existing agreement, BfR cannot in any way distribute to third parties, national and international, information, communications, reports, publications about the specific collaborative results of this project related to point 3 of Annex A within conferences and/or training courses.

The authorization request must be sent from ISS to the scientific advisor of the Italian Ministry of Health.

Authorized publication of the above information should include information on: "The project has been realized with the financial support of the Italian Ministry of Health – Direzione Generale per l'Igiene e la Sicurezza degli Alimenti".

Irrespective of the before-mentioned, BfR may publish the results without consent of the ISS in case such publication is required for enabling BfR to fulfill its legal tasks, in particular for its risk assessment and risk communication; BfR shall inform ISS thereof in writing within ten (10) days after the publication.

Article 8

(Payments suspension and agreement dissolution)

ISS will suspend the provision of the financing in the event of a negative evaluation of the reports referred to in Article 5, or for failure or irregular implementation of this Agreement.

In case of detection, in the examination of the reports provided in Art. 5, of serious breaches to the obligations set in this Agreement that may affect the implementation of the project, for reasons attributable to BfR, ISS can give notice to put an end to the violation within a stipulated period by writing to BfR, by means of registered letter with advice of delivery or equivalent. Exceeded the time limit, the Agreement is cancelled with effect from the date indicated in the notice.

The agreement is solved also in the case of failure by BfR to submit reports within the prescribed time limits.

It is expressly agreed that in the event of termination of this Agreement, BfR has an obligation to provide, within 60 days from the receiving of the related request, to refund of the sums paid until the date of the Act termination.



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Article 9
(Responsibility and Court of Justice)

In the event of a dispute in the interpretation or execution of this Agreement, the matter will be settled through friendly negotiation in the first instance. If this is not possible, the competent court of justice will be the Tribunal of Rome.



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Article 10
(Registration and stamp duty)

This Agreement, drafted in the form of unauthenticated private agreement, is subjected to registration only in case of use. The related expenses shall be in charge of the requesting party.

Stamp duty is paid in virtual mode to exclusive care of the Institute (license # 99718/2016 of the Revenue Agency – D.R. Lazio).

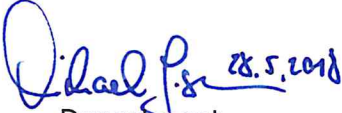
This Act drafted in two original copies is read, approved and signed by electronic signature and will be recorded only in case of use, by and at the expense of the requesting party.

For ISS:


Director of
Human and Economic Resources
(Dott.ssa Rosa Maria Martoccia)

12.06.18

For BfR:

J.A.  28.5.2018
Head of the Department
Administration
(Mr. Michael Gose)



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ANNEX A – Executive project

For the realization of the objectives of the project "Virus dell'epatite E nelle carni suine fresche e conservate" [Hepatitis E viruses in fresh and cured meat], ISS and BfR will develop their cooperation through the following activities:

1) Acquisition by ISS of an *in vitro* cultivation system for HEV:

For this activity BfR will provide to ISS, through international shipment at controlled temperature, the viral strain of HEV number 47832c and the optimized subclone cell culture system A549 (A549 / D3). A viral stock of strain 47832c for supporting initial experiments and to allow test of HEV viability will be provided together with cell subclone A549 / D3. Cell line N5-A549/HEV (persistently infected with strain 47832c) will also be provided to support preparation of HEV virus stocks.

2) Training and assistance in the implementation of the *in vitro* cultivation system for HEV:

BfR will provide specific training to one unit of personnel of ISS for the correct implementation of the culture system and for virus quantification through titration and subsequent immunofluorescence assay. Standard operating procedures will be provided during the training together with indications on required reagents.

3) Assessment of EMA/PMA rt-RT-(q)PCR of HEV:

BfR will cooperate in the performance assessment of the EMA/PMA rt-RT-(q)PCR of HEV to be developed within the project by supporting the comparison of the result of the molecular method in comparison to the cell culture assay. To this aim, ISS will share the results of the two assays with BfR, protocol optimization will be agreed and statistical analysis will be jointly reviewed.



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Budget

	Amount
Consumables	18.000,00
Overheads	0.000,00
Total	18.000,00