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	Standard operating procedure of the Hp-EuReg study	
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STANDARD OPERATING PROCEDURE OF THE STUDY "EUROPEAN REGISTRY ON *HELICOBACTER PYLORI* MANAGEMENT" (Hp-EuReg)

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EUROPEAN REGISTRY ON *HELICOBACTER PYLORI* MANAGEMENT (Hp-EuReg)

The "European Registry on the Management of *Helicobacter pylori* Infection" (Hp-EuReg) is a prospective, non-interventionist, multi-centre study initiated in 2013, and promoted by the European Helicobacter and Microbiota Study Group (EHMSG).

This project, which brings together more than 200 researchers from 29 European countries, evaluates the current clinical practice of European gastroenterologists on the management of *Helicobacter pylori (H. pylori)* infection, allowing the implementation of clinical recommendations agreed by the scientific community, through continuous evaluation and design of improved therapeutic strategies.

The rate of patient inclusion in the Hp-EuReg averages between 6,000 and 8,000 patients per year overall and this registry represents the most extensive dataset on *H. pylori* management in the world.

The high scientific production of the Hp-EuReg has resulted —and continues to do so— in the publication of numerous conference communications and Journal articles.

Since the inception of the study in 2013, there has been a 10% increase in the overall effectiveness of first-line treatments, representing a very significant finding, as it is estimated that over 50% of the world's population is infected with *H. pylori*. In addition, the Hp-EuReg allows to comply with the European

guidelines on monitoring the responsible use of antibiotics, contributing to avoid the uncontrolled increase in bacterial antibiotic resistance.

Furthermore, the results of the Hp-EuReg not only have a beneficial impact on the scientific community and society —including other disease areas, but also on each researcher curricular itinerary. Thus, the contribution of a significant number of patients ensures, as collaborating researcher, authorship in the publications. In addition, the Hp-EuReg Scientific Committee encourages researchers to lead any sub-study they wish to conduct, and therefore researchers can also benefit from local publications.

Finally, it should be noted that the Hp-EuReg has its own website (http://www.hpeureg.com/), where all the up-to-date clinical information may be consulted at any time, as well as the participation rate of each country and the latest news regarding conference communications, articles, awards and interesting analyses in the spotlight, among others.

OBJECTIVE

This Standard Operating Procedure (SOP) is intended to ensure the correct pathway for participating, recruiting patients, consulting and evaluating data, preparing studies and disseminating the Hp-EuReg project results.

By agreeing to participate in the study, investigators make a commitment to the Scientific Committee and the other investigators, taking an active part in patient inclusion, promoting participation with other gastroenterologists or centres that may become involved, and disseminating the project in order to encourage active patient recruitment. Active participation is necessary in order to keep the registry in optimal conditions for future analyses.

Participating researchers can commit at different levels. The different roles and responsibilities (rights and obligations) of each are described below.

DEFINITIONS

Roles

The different roles in the Hp-EuReg have been established by hierarchical order, from greater to lesser responsibility level, as stated below.

Principal Investigator (PI): Head of the study, maximum responsible of any action derived from it. The PI manages the development of the Hp-EuReg research project at all levels. The PI promotes, controls and evaluates the functions and activities of the co-investigators. The PI is also involved in research proposals aiming at the search for financing as well as devising new potential lines of research. Finally, the PI designs studies and supervises analyses, research results and manuscript production.

Hp-EuReg Scientific Committee: Currently composed of six members, including the PI and two scientific directors. This steering committee contributes to the design of the main study (and sub-studies), and acts as the project's decision-maker at all levels including: supervision of data inclusion, follow-up, monitoring, quality reviews, statistical analyses, drafting of manuscripts, definition of authorship policy as well as decision on the status of the researchers within the project. Researches are subject to continuous evaluation of their activity, which determines whether they are allowed to continue or should leave the study if participation criteria are not met.

Scientific Director: In the Hp-EuReg there are two profiles. One of them is mainly focused on the clinical and methodological aspects of the study such as study designs, protocol development, statistical analysis of the data, data

management, data quality review, study design and manuscript drafting. The other profile is focused on the strategic dissemination of the project from a networking and communication management standpoint. These two management aspects are also shared with the PI, including tasks as supervision of the participation procedure; encouragement of participation plan; guidance in the patient recruitment process and data evaluation providing technical and scientific support in all aspects of the Hp-EuReg as well as in the communication area (study presentations at congresses, manuscript publication) through the relevant channels (Twitter, research centres, among others).

Technical Project Manager: Responsible for the presentation of summary reports, preparation and sending of quarterly *newsletters* of the registry. The technical project manager is responsible for the maintenance of the website, Twitter account and Google Analytics. The technical project manager is also in charge of sending the invitation for participation in the study, the registration and inclusion of the investigator in the corresponding centre and verifies that the researchers meet the requirement criteria for participation. Moreover, the technical project manager is also responsible for monitoring the activity of the researchers. Finally, the technical project manager is in charge of the maintenance and management of the database, in collaboration with the Hp-EuReg Scientific Committee, implementing measures for its improvement

National Coordinator (NC): The NC acts on behalf of the Hp-EuReg Scientific Committee and is the main national contact for recruiters and the Scientific Committee. The NC is responsible for the selection of sites and the correct participation of researchers. NC tasks are to attract and retain recruiters;

to oversee and promote prospective inclusion of patient data reflecting routine clinical practice; and to monitor the eCRF to ensure data quality. The NC can also promote studies with local data from her/his country and suggest ideas regarding the whole database (the Scientific Committee will assess the suitability of the NC to lead such studies).

Regional Coordinator (RC): The RC is the investigator responsible of a specific area of a country. The RC leads a group of participating hospitals/investigators within a county and has, at the practical level, the same tasks as the NC to whom the RC reports.

Recruiting Investigator (RI): Investigator recruiting patients and registering them in the e-CRF AEG-REDCap platform (see definition below). The RI must be a gastroenterologist from any type of centre (e.g., tertiary hospital, specialized centre, public, private, among others) where *H. pylori* infected patients are treated.

Other definitions

REDCap: stands for “Research Electronic Data Capture” and is a secure web platform for building and managing online databases and surveys offering a wide range of tools that can be tailored to virtually any data collection strategy. The software enables the design, development and management of electronic case report forms (CRFs) for data collection in basic or clinical research studies, including multicentre, prospective or randomised trials. In addition, it provides the necessary tools for efficient data analysis, real-time descriptive statistics, monitoring through querying system, data collection on mobile devices, API

access for advanced analysis; emailing and additional features on data management.

AEG-REDCap: online collaborative research platform provided free of charge by the Spanish Association of Gastroenterology (AEG, Asociación Española de Gastroenterología) with the sole aim of promoting independent investigator driven research. Data of the Hp-EuReg is hosted at AEG-REDCap.

e-CRF: electronic case report form.

DAG: stands for "Data Access Group". Data access groups restrict the viewing of data within a database. A typical use of DAGs is a multi-site study where users at each site can only view data from their site, but not any other sites. Thus, users at each site are assigned to a group and can only access records created by users within their group. The DAG acts as a default security system within the platform, ensuring data protection.

Instrument: section of the e-CRF in REDCap that compartmentalises the information of the study, collecting the different variables.

Record ID: Identifier of a record (de-identified code) in the Hp-EuReg REDCap database.

Active participation: the desirable objective is to include as many patients as possible according to each geographical context (e.g., prevalence of infection, care possibilities, etc.); complying with a minimum of 50 records per researcher per year. The success of the project lies in the continuity of the inclusion of patients, which allows evaluating trends of outcomes over the years.

PARTICIPATION IN THE HP-EUREG

The steps of the Hp-EuReg participation process are:

a. Invitation to participate (Annex 1)

First, an email with an invitation from the PI (see Annex 1) and the Scientific Committee will be sent to the interested researcher, carbon copying the NC of the country, the PI and the scientific directors. This invitation contains: relevant information of the Registry; a generic username and password allowing to browse a copy of the actual database; name of the NC and the authorship policy. It also contains a link to the application form (Annex 2): https://redcap.link/fbrdl6t1, where the interested researcher can fill in the form with personal and contact details: name and surname, e-mail, recruitment centre/s, city and country.

The researcher can gain access to the project through different channels:

1. By contacting the county NC.
2. By contacting the Technical Project Management directly (acano@aegastro.es) or any of the other projects´ members.
3. By accessing the website www.hpeureg.com, where a “Join the project” button links directly to the application form (Annex 1).

It should be noted that if more than one researcher of a centre is interested in participating, then an individual application for participation is required, so that on one hand, each investigator has her/his own *signing in* credentials, and on the other hand, a participating traceability is available for each user. This traceability

will then contribute to include the authorship byline in each manuscript (see Authorship Policy).

b. Registration on the AEG-REDCap platform and Hp-EuReg

Once the online application form is completed, the technical director automatically receives the researcher's data via the AEG-REDCap platform, where the researcher is registered as a new user (it is advised checking whether a given investigator applying to participate in the Hp-EuReg study previously signed up in the REDCap platform as part of another project, in order to avoid duplicated users), and thereafter, signs up in the role of recruiter in the Hp-EuReg.

c. Access to the AEG-REDCap platform and Hp-EuReg

Once the technical director completes the registration process, the researcher will receive four emails:

1. An automatic email generated by REDCap when a new user is created and registered in the platform for the first time.
2. An automatic email generated by REDCap when the researcher is assigned to its role as part of the Hp-EuReg project.
3. A welcome email to AEG-REDCap (Annex 3) sent by the platform administrator, confirming that the researcher has been registered and recalling reception of the automatic email mentioned in the first point above, where a link to activate a provisional password is available.
4. A welcome email to the Hp-EuReg project (Annex 3) sent by the technical director of the Hp-EuReg, including the information access to the Hp-

EuReg project —Affiliations and COI— where the researcher is deemed to include the data required for authorship. The email also includes the invitation to visit the project website: www.hpeureg.com.

5. If deemed necessary by the technical director, the researcher will be invited to use a project with "dummy" patients so that each instrument and variable of the e-CRF can be properly understood.

d. Inclusion of patients in the CRF

The e-CRF contains six instruments, which collect different information (see full e-CRF in Annex 4).

1. **Baseline demographics**: Country/Centre; self-numbered patient identification number; gender and date of birth; ethnicity; drug allergies; relevant comorbidities; current concomitant medication.
2. **Medical condition**: Indication for diagnosis and treatment; upper GI symptoms; diagnostic test.
3. **Previous eradications**: Number of previous eradication attempts and treatment scheme(s) previously prescribed.
4. **Current treatment**: Regimen, drugs; dosage; duration.
5. **Adverse events**: Type of event, intensity, duration and relationship to treatment; discontinuation of treatment due to adverse effects.
6. **Outcome**: Treatment compliance; result of the eradication confirmation test (yes/no); test used and date.

e. Rights and duties of researchers

Hp-EuReg researchers are committed to active and quality participation, which entitles them to a number of rights as outlined below:

- They will have a username and password to access the AEG-REDCap platform. The credentials allow them to access all the records assigned to their DAG within the Project for their personal or academic use.
- They will be entitled to authorship in the communications and publications derived from the study (see Authorship Policy).
- Partial studies or local analyses of the database may be carried out for publication after approval by the Scientific Committee (see Statistical analysis request).

In return, the Hp-EuReg recruiters should commit to:

- Maintain their active participation. The desirable target is to include a minimum of 50 patients per investigator per year.
- Include quality data. Researchers are deemed to complete all fields of the e-CRF in order to avail statistical exploitation and data mining.
- Communication between the different parties should be fluid, especially between their respective NC and the Hp-EuReg Scientific Committee.

DATA PROTECTION

The processing, communication and transfer of personal data of all participants (both researchers and patients) will comply with the EU Regulation 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealed Directive 95/46/EC (General Data Protection Regulation) as well as with the Organic Law 3/2018 of 5 December on the Protection of Personal Data and guarantee of digital rights.

The data for this study will be collected and registered by a single de-identified code (Record ID), without possibility of establishing a link to any participant information. The patient's date of birth and date of visit will be included in the record as the database variables' identifiers, but only the responsible physician(s) with access rights to the medical records will be able to link such information with a patient's name; and thus, records will remain anonymous for any REDCap user.

Access to personally identifiable information may be granted to health authorities, the Research Ethics Committee and personnel authorized by the study sponsor, when necessary to verify study data, for specific auditing or any other procedures, but always maintaining confidentiality in accordance with the current legislation.

Only encrypted data will be disclosed to third parties and other countries, and will not contain in any case information that could directly identify the participant.

EVALUATION OF RESEARCHER PARTICIPATION

Quarterly systematic monitoring is performed by the technical project manager on the participation of the individual recruiters, measured as the number of newly included patients by investigator. Please refer to the SOP " Strategy for inactive users" (Annex 5).

The purpose of this monitoring is to maintain and ideally increase the rate of patient inclusion. The monitoring is performed in two steps:

- By reminding the recruiters they should continuously include patients, after confirming three months of user inactivity (i.e., no patient included).
- By giving notice of user inactivity after confirming one year without patient inclusion.

How is it done?

1. By sending an e-mail to those inactive users who have not registered any patient in the last three months encouraging them to boost their participation (see Rights and Obligations).
2. By sending an e-mail to those inactive users who have not registered any patient in the last year informing them that they will be suspended from the study in two months, unless reactivation takes place. After the two-month allowance period (and without request of further extension), should no patient be included, the recruiter will finally be suspended from the study (i.e., access to their corresponding DAG and data will be revoked) and

notified by email. However, the suspended researcher can request at any time in the future an account re-activation to re-start participation.

EVALUATION OF DATA QUALITY

In order to maintain homogeneity of the collected data, as well as to maximize their use in statistical analyses, the Scientific Committee decided to make a selection of the most relevant variables of the e-CRF that would need to be completed in full. These variables are requested to be filled in correctly in order to increase the number of high-quality records for analyses.

This monitoring of data quality is performed firstly through a strategy in REDCap by means of an advanced “real-time” report which will detect all records with missing information on the following variables:

1. Line of treatment
2. Prescribed regimen
3. Duration of treatment
4. Prescribed drugs
5. Adherence to treatment
6. Result of post-treatment diagnostic tests (positive or negative)
7. Confirmation of eradication (success, failure or lost to follow-up) by the prescribing physician.

The technical project manager will contact the investigators (NCs or investigators of the corresponding DAGs) for appropriate data correction on a quarterly basis.

Ultimately this will increase the number of complete high-quality records, which will allow to perform more in-depth statistical analyses.

Researchers should remember that only those records validated for statistical analysis will be taken into account in the authorship and acknowledgements of manuscripts.

Secondly, an additional review of data will be performed after each data extraction, reviewing at least 10% of the included patients. This second-level data review process evaluates whether the study selection criteria were met, whether information was correctly registered and ultimately to ensure the study was conducted according to the highest scientific and ethical standards.

Additionally, prior to statistical analysis, data will be reviewed for inconsistencies mainly on the variables described above checking for further detail. Subsequent data cleaning will be performed.

Data discordances will be resolved by the technical project manager querying the investigators and through group emailing.

DATA ANALYSIS

A statistical evaluation and scientific-medical synthesis of the Hp-EuReg overall data collected will be performed every sixth months by the Scientific Director.

Specific systematic analyses will be performed on prescriptions, compliance, effectiveness and safety of treatments.

Additionally, these datasets will contribute to the data quality evaluation process mentioned in the corresponding section.

a. Periodic evaluation of data

The Scientific Committee decided to perform two data extractions, approximately in January and June, on the overall data (including all European countries and DAGs). The Committee established that this twice a year evaluation of the overall dataset was sufficient to reflect changes in *H. pylori* clinical management over time.

The analyses will focus on treatment prescriptions from 1st to 6th line, evaluating the effectiveness, safety and compliance. Data will be analysed systematically, stratified by region and/or country and evaluated over the years (temporal trends).

This task will be led by the Scientific Director in charge.

b. Data management for statistical analysis

A priori definitions have been established to ease the analysis and interpretation of the information collected. Below is detailed how data on the

effectiveness of treatments, their duration or the dose of proton pump inhibitor (PPI) used, are managed. Further specific and tailored data management methodology required in each study will be specified in the methods sections of the published manuscript, as appropriate.

The main outcome used to evaluate the effectiveness is the eradication rate (variable “efficacy” of the e-CRF) achieved with the treatment. Confirmation of eradication should be performed at least one month after completing the treatment with at least one of the following diagnostic methods: urea breath test, stool antigen test and/or histology.

The intention-to-treat (ITT) analysis will include all patients registered up to 6 months before the data extraction date to allow the patient/investigator enough follow-up time to register the post-treatment result. In the ITT set, lost to follow-up cases will be deemed as treatment failures.

The per-protocol (PP) analysis will include all cases that had a complete follow-up (that is, those who had a post-treatment test result checked with the “efficacy” variable, either as “success” or “failure”) and achieved at least 90% treatment compliance (compliance is selected as “yes”). If the eradication success is not confirmed, these records will simply not be taken into account in the PP set.

The modified ITT (mITT) group will aim to reflect the closest result to that obtained in clinical practice; therefore, this analysis will be basically the same as the PP but will include all cases that had a complete follow-up (i.e., those that had undertaken a confirmatory test after the eradication treatment), regardless of compliance (meaning it also includes those patients with poor compliance, so the

variable “compliance” can be “yes” (1) or “no” (2). Likewise, as in the PP set, if the eradication success has not been confirmed, these records will simply not be taken into account in the mITT set.

PPI doses will be categorised according to the potency of acid inhibition, as low-dose (4.5–27 mg of omeprazole equivalents given twice a day), standard-dose (32–40 mg of omeprazole equivalents given twice a day), or high-dose (54–128 mg of omeprazole equivalents given twice a day).

Likewise, the duration of treatment will be categorised as 7, 10, or 14 days (most frequent treatment lengths) to ease interpretation.

c. Statistical analysis request

Should an investigator request a statistical analysis for a given study (could be at a local level, that is for a specific country, or a study encompassing the overall European data), the application will need to include a protocol of the planned study detailing: the objective(s); the variables of interest in the analysis (highlighting line, treatments to be explored, population, etc.); whether methodological or statistical support is required; and timelines (i.e., a brief chronogram) for manuscript production.

Requests will be addressed to the Scientific Director in charge, Dr. Olga P. Nyssen (opn.aegredcap@aegastro.es), who will provide the results in due course and will be involved in all phases of the analysis and interpretation of data as well as in manuscript production and peer review, in agreement with the Hp-EuReg Scientific Committee.

d. Scientific production

Hp-EuReg data syntheses are regularly reported in the form of abstracts, congress oral presentations, and conference proceedings as part of national and international meetings, as well as manuscript publications in Gastroenterology or health-related journals.

AUTHORSHIP POLICY

The authorship statement applies both to conference abstracts and manuscripts published in journals (see Researchers' rights and obligations).

Authorships are written in strict order of country and researcher participation, according to the number of patients included in each centre (DAG) and taking into account each study aim (nota bene: each study will vary in the number of patients analysed according to the specific study question; therefore, the number of participating countries, DAGs and ultimately investigators involved, will be different in each case and in some cases no authorship will be granted):

- The number of authors on the cover page of the article shall be a maximum of 50 (threshold established as per usual Journal space restrictions).
- In each particular study, only the NCs of the countries participating in that specific study will be included, always at the end, and before the members of the Scientific Committee.
- The order of the NCs will depend on the participation of each country in each specific study.
- The order of inclusion of the researchers will be based on the strict criteria of participation of their DAG (regardless of the country) from higher patient inclusion rate to lower.
- If there is more than one researcher in each DAG, the lead researcher of the aforementioned DAG (top recruiter measured as per the highest number of patients collected) will be placed first, adding the second (and

successive fellows, if any) behind their corresponding lead researcher, until all positions are completed.

- The position of the regional coordinators (in Spain) will depend on the level of fulfilment of their responsibilities and commitment, and will be subject to the criteria of the Scientific Committee.
- The remaining investigators participating in the study, not included in the cover page, will be included and listed (also by DAG participation order) in the supplementary material file called “Hp-EuReg investigators” which will be referred in the article as to *On behalf of the Hp-EuReg investigators* at the end of the authorship byline. This, to all intents and purposes, grants the investigators the same level of authorship in the given manuscript as the authors in the front page.
- Those researchers who are no longer participating in the registry and are inactive at the time of data extraction of the study, will not have the right to authorship; except those with a particularly relevant contribution to the specific study (e.g., sufficient number of recruited patients in the past), they will be included in supplementary file with other contributors, but this decision will be subject to the criterion of the Scientific Committee.

Before submitting any Congress communication or manuscript publication, the Hp-EuReg Scientific Committee will send the manuscript to all researchers for their final critical review. In this way, 1) the researcher will always be informed of the studies derived from the Hp-EuReg; 2) the researcher will be able to verify whether her/his authorship and affiliation are correct and/or claim her/his

authorship if not included; 3) the researcher will be able to critically review the manuscript.

In communications to congresses, all those researchers who have participated in a given study and whose name cannot appear on the title page (due to space limitations), may request, if necessary, a certificate of authorship at: acano@aegastro.es, once the Congress has taken place (and abstracts are published).

PROMOTION AND DISSEMINATION OF THE PROJECT

The Scientific Director, together with the technical project manager, has direct and personal contact with all NCs to help them promote the study in their country. This Scientific Director will assess local participation together with the NC, by analysing causes of inactivity and based on the experience in other countries, by helping the NC with specific strategies to encourage recruitment and boost regional participation. Below is listed the step-by-step main strategy to increase recruitment:

- To explain the project using mainly the information on the Registry's website: www.hpeureg.com.
- To give the researcher access to a copy of the project hosted at AEG-REDCap created for training purposes. This way the variables of the database can be explored and “dummy” patients can be registered for a better understanding of the information that will need to be collected:
    - Link: Hp-EuReg Training (https://redcap.aegastro.es/redcap_v12.3.2/index.php?pid=108)
    - Username: practice
    - Password: Practice1234
- To emphasize the ease of including patients in the database, highlighting that it takes no more than five minutes to enrol a patient and fill in the database.

How can I invite gastroenterologists to participate in Hp-EuReg?

- By sending an e-mail to all members of national gastroenterology associations in the given country (examples of e-mails can be provided upon request).
- Presenting the Hp-EuReg at national meetings. The NC can present global and local Hp-EuReg results. The Scientific Committee will provide a power point presentation template to help the NC in this task.
- Searching PubMed for gastroenterologists in the given country who have published articles on *H. pylori* in the last five years.
- Building a list of potential new investigators. The NC will be advised to recruit potential investigators willing to develop their scientific career and improve their CV, as well as senior leaders who may not be involved in the recruitment of patients, but may be involved in the recruitment of gastroenterologists that could be potentially selected from their research group, medical societies, or any other valuable network in which they might be associated fellows.

COMMUNICATION PLAN

Dissemination channels

- Web www.hpeureg.com.
- Twitter @hpeureg.
- *Newsletters*.
- Partnership

1. **www.hpeureg.com**

   The website will be updated quarterly. What should be updated?

- Latest featured publication
- List of published articles
- List of manuscripts in preparation
- List of abstracts presented at national and international conferences
- Featured new items
- Graph of number of patients included per year
- Graph of number of patients included by country
- Graph of participation by country in the last three months
- Graph of most frequent first-line and recue treatment prescriptions
- Graph of the evolution of first-line treatment effectiveness
- Graph of the evolution of second-line treatment effectiveness

2. **Twitter @hpeureg**

Project profile for the dissemination mainly of interesting news, meetings, conferences, and analysis. It is intended to help building corporate branding and increasing participation. It might also potentially help to the globalisation of the Hp-EuReg. The twitter profile will allow:

- To interact with professionals and entities in gastroenterology (Key opinion leaders, scientific societies, networks, etc.).
- To spread important Hp-EuReg content:
    - Published articles.
    - Participation in conferences and congresses.
    - Interesting analyses (e.g., graphs of most commonly used treatments and their effectiveness/safety profile).
- Awards
- To disseminate personal accounts content (retweets).
- To disseminate relevant activities of the field.
- To recommend third-party contents.

3. Newsletter

Sent quarterly. It will include:

- The list of the last 10 publications.
- The graph of the overall participation.
- The graph of the participation by country.
- The graph of the participation by country during the last three months.
- The graph of the top recruiters.
- The graph of the number of patients included per DAG in each country.

4. Partnership

Communications (in the form of newsletters, e-mails or web articles) through the entities associated in some way with the Hp-EuReg, mainly: the European Helicobacter Study Group (EHMSG), Hospital de La Princesa, Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Althaia Xarxa Assistencial Universitària de Manresa, the Spanish Association of Gastroenterology (AEG), and collaborators of the World-Wide Registry on *H. pylori.*

ANNEXES

Annex 1. Invitation to the Hp-EuReg: letter template

European Helicobacter & Microbiota Study Group

Hp EuReg

AEG REDCap

European Registry on *Helicobacter pylori* Management

Dear Dr,

On behalf of Dr Javier P. Gisbert, Principal Investigator of the **European Registry on *H. pylori* Management (Hp-EuReg)**, I am glad to invite you to participate in this project.

Please, join the Hp-EuReg by completing the user form following the survey link in your web browser: https://redcap.link/fbrdl6t1
*****PLEASE DO NOT USE A HOTMAIL ACCOUNT TO SIGN UP, AS REDCap DOES NOT SUPPORT SUCH SERVER. THANK YOU****

You will then receive (within less than one week) to the email address provided your credentials to access the database and start including patients straightforward.

For additional information, please visit our website at www.hpeureg.com which is periodically updated with the most up-to-date Registry news.

Please find below the invitation e-mail from Dr. Gisbert.
Best regards,

Anna Cano-Català
Technical Project Manager
European **Reg**istry on **H**elicobacter
pylori Management (**Hp-EuReg**)
www.hpeureg.com

Dear Dr,

I am writing to inform you about a project promoted by the European Helicobacter and Microbiota Study Group called "**European Registry on *H. pylori* Management (Hp-EuReg)**". Thanks to the electronic case report form (e-CRF) created, we are ready for new participant centres and researchers, and we would like to invite you in.

Some FIGURES of the study:

- More than 200 researchers from 29 European countries are currently participating
- More than 50,000 patients have been included to date
- High international recognition with 6 international awards by the UEG and the EHMSG
- In 2021 and 2022, 13 articles were published, and 18 more are currently in preparation
- More than 20 abstracts were accepted in the last EHMSG and UEGW workshops

What is the AIM?

To prospectively register all patients treated for *H. pylori* infection. This will allow the evaluation of many factors involved in *H. pylori* eradication. The study has been prolonged with no definite end, as we also aim to perform time trend analyses. The project also allows individual researchers (recruiters) to perform partial or local analyses (and to publish them) after approval by the Hp-EuReg Scientific Committee (Javier P. Gisbert, Francis Megraud, Colm O'Morain), currently also integrated by the Scientific Directors (Leticia Moreira and Olga P. Nyssen).

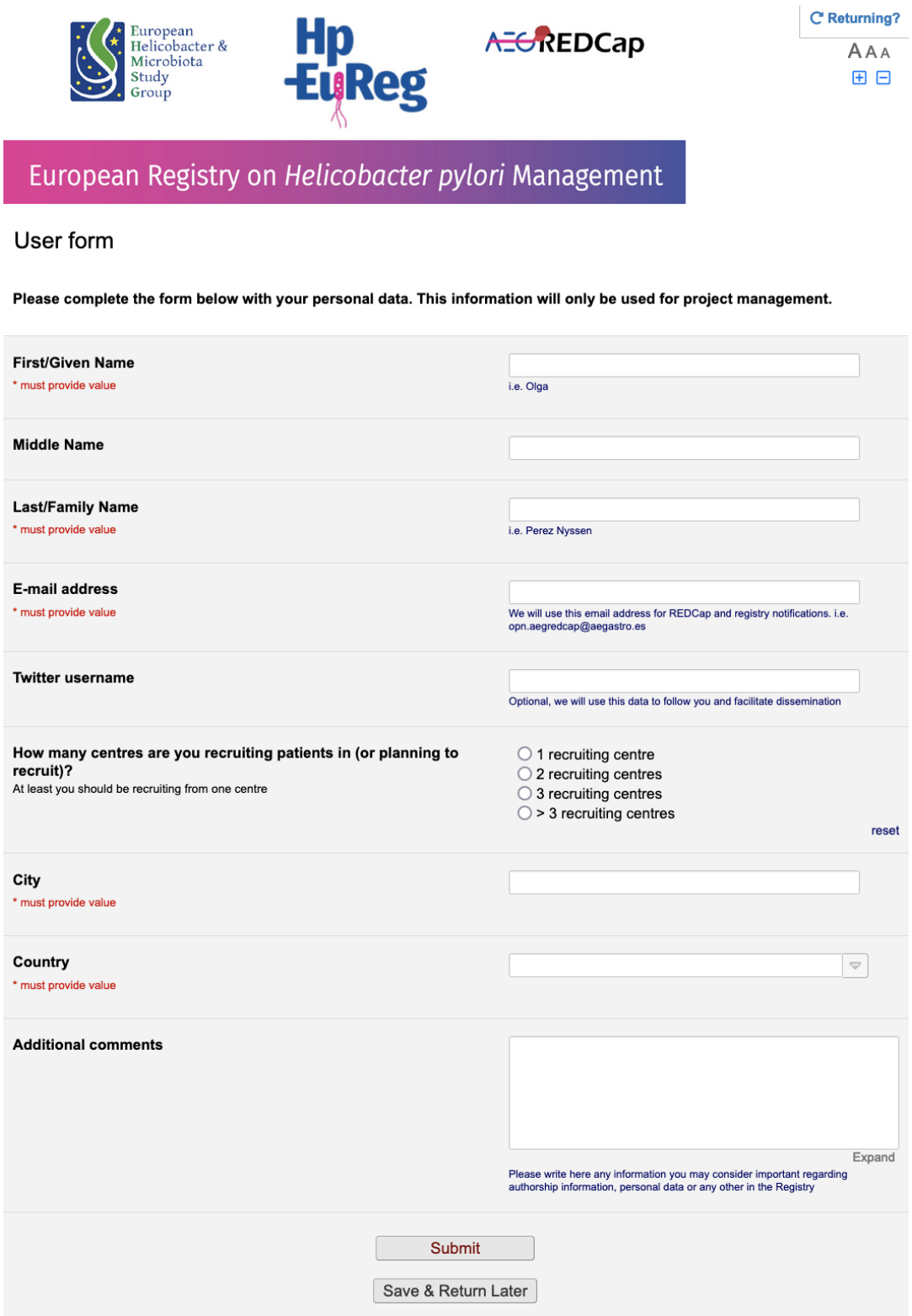
How will the project increase your CURRICULA?

All contributions will be listed in publications to allow you to include them in your Curricula as original work. Authorship entitlement and the contribution order in publications, will be based mainly on the amount and quality of your participation. Additionally, all participant researchers will be able to perform partial or other specific studies in the database where first- or senior co-authorships will be granted to those suggesting or promoting the research.

Who is your National Coordinator?

Your National Coordinator for COUNTRY is Dr ....., and is your main contact person in case of any doubts or questions.

Annex 2. Application form



European Helicobacter & Microbiota Study Group

Hp EuReg

AEGREDCap

Returning?

AAA

European Registry on *Helicobacter pylori* Management

User form

Please complete the form below with your personal data. This information will only be used for project management.

First/Given Name
* must provide value
i.e. Olga

Middle Name

Last/Family Name
* must provide value
i.e. Perez Nyssen

E-mail address
* must provide value
We will use this email address for REDCap and registry notifications. i.e. opn.aegredcap@aegastro.es

Twitter username
Optional, we will use this data to follow you and facilitate dissemination

How many centres are you recruiting patients in (or planning to recruit)?
At least you should be recruiting from one centre
- 1 recruiting centre
- 2 recruiting centres
- 3 recruiting centres
- > 3 recruiting centres

reset

City
* must provide value

Country
* must provide value

Additional comments
Expand
Please write here any information you may consider important regarding authorship information, personal data or any other in the Registry

Submit

Save & Return Later

Annex 3. Welcome mails to AEG-REDCap and the Hp-EuReg project

Dear Dr ,

As requested by *Javier P Gisbert*, principal investigator of the project "*European Registry on H. pylori management (Hp-EuReg)*", I have sent you an email with your access information to log in the Collaborative Research **Platform AEG-REDCap**, the data management tool used to access the Hp-EuReg database.

The access emails are sent to your email address using an **automated email** (bot) to ensure data confidentiality (no one has access to your password). However, this bot may be identified as spam by the security controls of the email server.

If you do not find it in your inbox, it may have been classified as unwanted mail (**spam**), so please **check the spam, junk, trash and/or filtered mail folders** applicable to your server. Beware that each server uses its own naming and classification system, so the name of the folder/s may depend on the server or program.

If you are still unable to find it, please use the internal search tool of your email server (a tool that is provided by most servers and programs). You may search the terms "REDCap" or "soporte.aegredcap@aegastro.es" o Anna Cano (AEG-REDCap administrator) "acano@aegastro.es", making sure that the search tool looks through all the folders (included spam and trash).

If, after all this**, the email does not appear**, it probably means that your server has a **complete blocking** of bot mails (which is the case of **Hotmail**). In this case, the best option is to give us an email **address on another server**, to reach you out in current occasions and also for future purposes such as password recovery or system notifications.

If you do not have any other email account, let us know, and we will use an **alternative hand method to provide you with the access information**. In any case, this hand system will not serve for the reception of system notifications, as it requires an effort on our side, and it is not recommended.

Best regards,

Anna Cano, on behalf of Olga P. Nyssen, Leticia Moreira, Javier P. Gisbert and the Hp-EuReg Scientific Committee

Welcome to AEG-REDCap European Registry on H. pylori

European Registry on *Helicobacter pylori* Management

Dear Dr ,

Welcome to AEG-REDCap and the European Registry on *H. pylori* Management (Hp-EuReg)!

We are pleased to count on your participation.

A recruiter account has been created for you in the project. If you did not have a previous REDCap account with us, you should also have received an email providing you with a username and password.

Now is the time to update your affiliation information in REDCap, which will be used for authorship statements in upcoming publications. Please, access the **Hp-EuReg - Affiliations and COI** project **(**https://redcap.aegastro.es/redcap_v10.0.4/index.php?pid=614**)** and register your data by clicking the button "Add / Edit Records" on the left-hand banner of the website.

We would also like to take this opportunity to inform you that the Registry has **Twitter account: @hpeureg**. We invite you to follow us so that you can keep up-to-date with the latest news about the project (publications, participation in congresses and conferences, interesting analyses...), as well as its members and participants.

Last, you can visit our website: **www.hpeureg.com,** which is periodically updated with the latest Registry information.

Should you have any doubts or questions regarding the software or the e-CRF, please contact **Anna Cano** (AEG-REDCap administrator) at: acano@aegastro.es.

Please, find enclosed a slide set presentation explaining the first steps in REDCap.

Best Regards.

Annex 4. eCRF

https://redcap.aegastro.es/redcap_v12.3.2/index.php?pid=432

You can access the e-CRF of the Training project via the link above, using the username and password below where you will be able to include dummy patients:

- Username: practice
- Password: Practice1234

Annex 5. SOP Inactive user registration strategy

HP-EUREG PROJECT - STRATEGY FOR INACTIVE USERS

Description and purpose

Maintain and ideally increase the rate of patient inclusion. The monitoring is performed in two steps:

- By reminding the recruiters they should continuously include patients, after confirming three months of user inactivity (i.e., no patient included).
- By giving notice of user inactivity after confirming one year with no patient inclusion.

Tasks planning

1. Sending emails:

- *1.1. Mail 1.* ***Directed*** **to those inactive users who have not registered any patient in the last three months**. To draw up a list of users who have not registered any new patient during the last three months. This information will be extracted from the project's logging, adjusting the filters with the event "record created (only)" and the corresponding date ranges.
- Exclude from this list those users who have been registered during the last six months. This can be checked by accessing the "Users management" project.
- Exclude from this list active researchers from the same centre who use a single user to enter patients in REDCap. We will not send them any more mail.

- Exclude from this list the researchers included in mail 2.
- Visually review the list, in case any further exceptions are detected.
- Encourage users who have not included any patients in the last three months to restart the inclusion as soon as possible.

1.2. Mail 2. ***DIRECTED TO those inactive users who have not registered any patient in the last year***. To create a list of users who have not registered any new patient during the last year. This information will be extracted from the project's logging, adjusting the filters with the event "record created (only)" and the corresponding date ranges.

- Exclude from this list those users who have been registered during the last twelve months. This can be checked by accessing the "Users management" project.
- Exclude from this list active researchers from the same centre who use a single user to enter patients in REDCap. We will not send them any more mail.
- Exclude from this list the researchers included in mail 1.
- Visually review the list, in case any further exceptions are detected.
- Send a friendly reminder email to the users of this listing stating that it is mandatory to reactivate their participation.

2. Termination of users

One month after sending mail 1:

- It will be verified that no new patients have been included within this month.

- It shall be verified that they have not requested any extraordinary grace period.
- The user will be suspended and notified by email.