# Planning a multinational H2020 Clinical Trial: experience & best practice from ECRIN

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EUROPEAN CLINICAL RESEARCH INFRASTRUCTURE NETWORK

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# TOPICS

overview

- ECRIN organisation and infrastructure - *brief overview*
- ECRIN involvement in H2020 projects and proposals - *experience*
- Budget calculation for the H2020 proposal - *essential information, tools, procedure*
- Time frame - *bottlenecks*
- Crucial topics - *diverging/different decisions in different projects*

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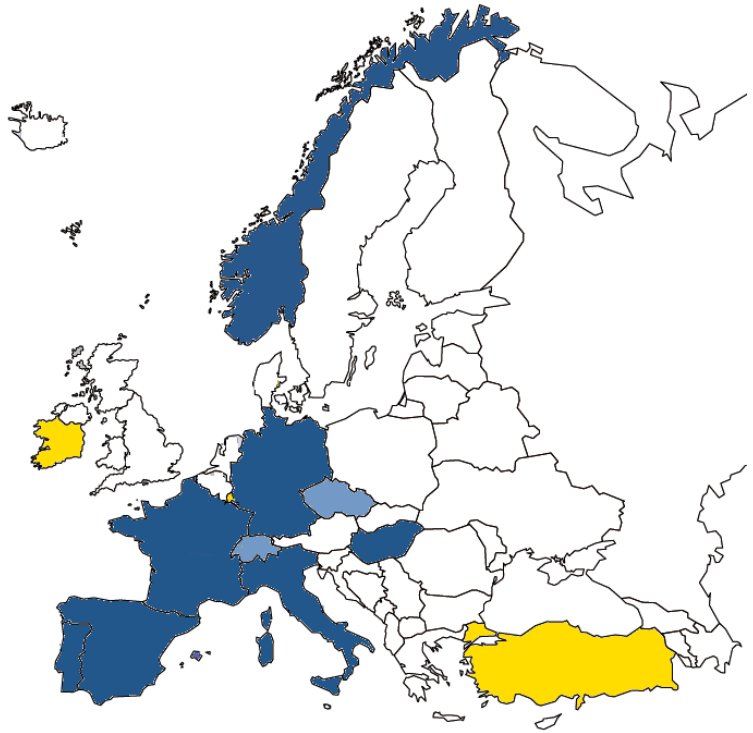
# ECRIN

## Overview

- A non-profit organisation with the legal status of European Research Infrastructure Consortium (ERIC)
- **Mission:** support the conduct of multinational clinical trials across Europe
- **Coordinated services from preparation to implementation**
- **9 Member and Observer Countries:** Czech Republic, France, Germany, Hungary, Italy, Norway, Portugal, Spain, Switzerland
  (additional countries about to join)



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# ECRIN - Organisation

## National Scientific Partners

- Czech Republic: CZECRIN – Czech Clinical Research Infrastructure Network
- France: F-CRIN – French Clinical Research Infrastructure Network
- Germany: KKSN – Netzwerk der Koordinierungszentren für Klinische Studien
- Hungary: HECRIN–Hungarian Clinical Research Infrastructure Network
- Italy: Istituto Superiore di Sanita (ISS), Rome
- Norway: NorCRIN – Norwegian Clinical Research Infrastructure
- Portugal: PtCRIN–Portuguese Clinical Research Infrastructure Network
- Spain: SCReN –Spanish Clinical Research Network
- Switzerland: Swiss Clinical Trial Organisation (SCTO)

# History At A Glance

- **2004:** ECRIN created; began 1st project (EU Framework Program 6, FP6) on strategy development involving six countries
- **2006:** 2nd project (FP6) on tools development with 12 countries; listed on European Strategy Forum on Research Infrastructures (ESFRI) roadmap
- **2008:** 3rd project (FP7) with 14 countries to develop ECRIN's business plan and legal status
- **2012:** 4th project (FP7), ECRIN Integrating Activity (ECRIN-IA), with 23 countries to structure national scientific partners and build their capacity to manage multinational trials
- **2013:** Awarded ERIC status
- **2016:** Listed as an "ESFRI Landmark"

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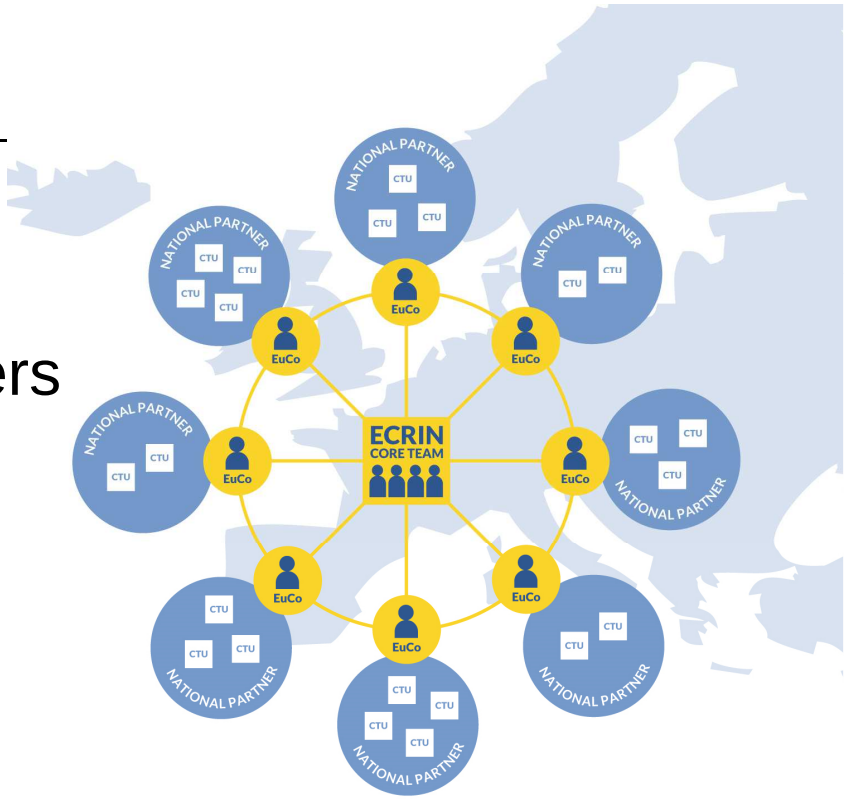
# Organisation: Distributed Infrastructure

EuCos, Core Team, National Partners

- **European Correspondents (EuCos)**
  - Implement work in-country in coordination with national partners
- **Core Team**
  - Develops ECRIN's strategy, common tools and procedures
  - Supports EuCos




- **National Partners** (networks of clinical trial units, CTUs)
  - Manage trials in-country and provide services to ECRIN
  - Host EuCos

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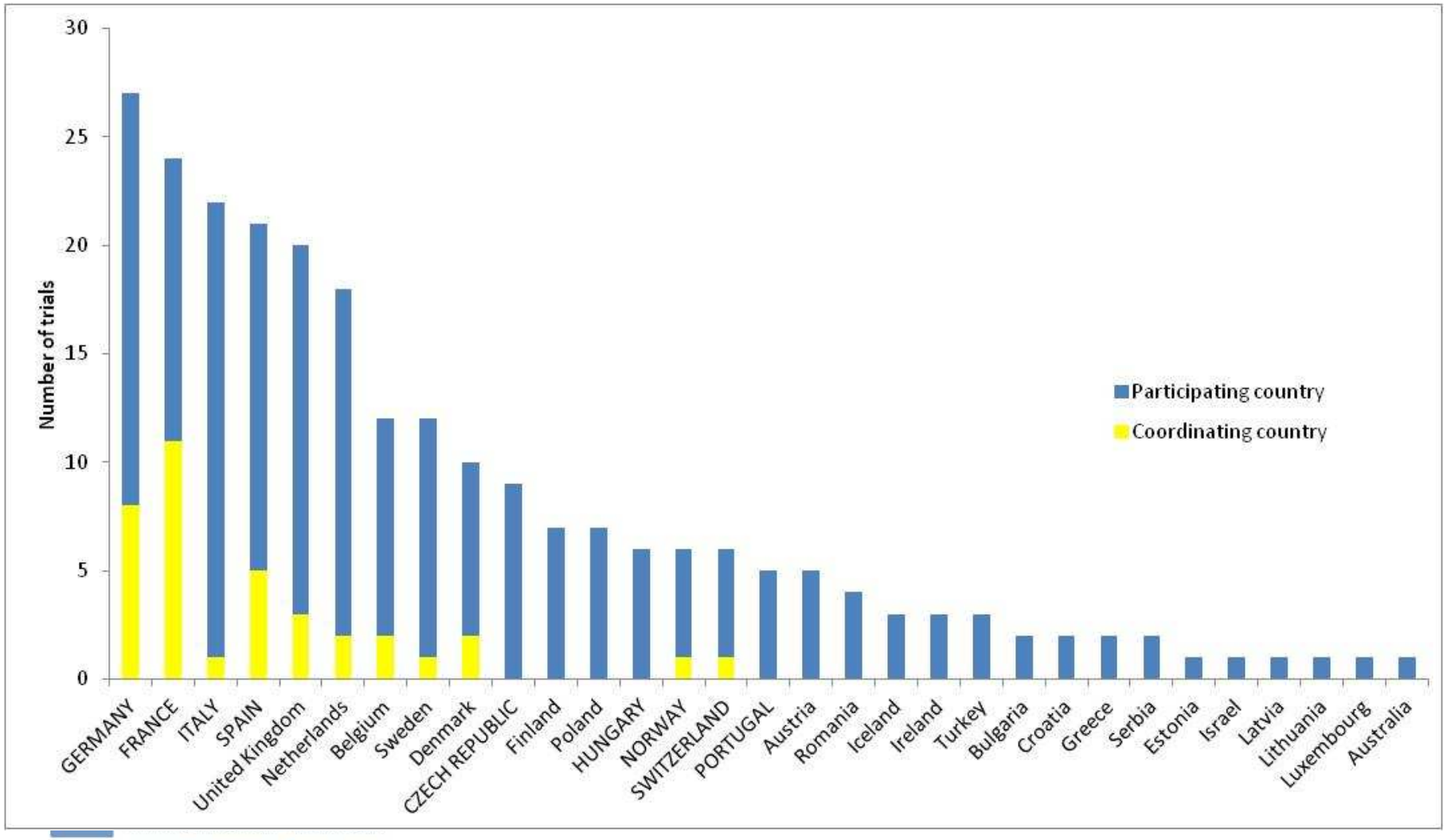
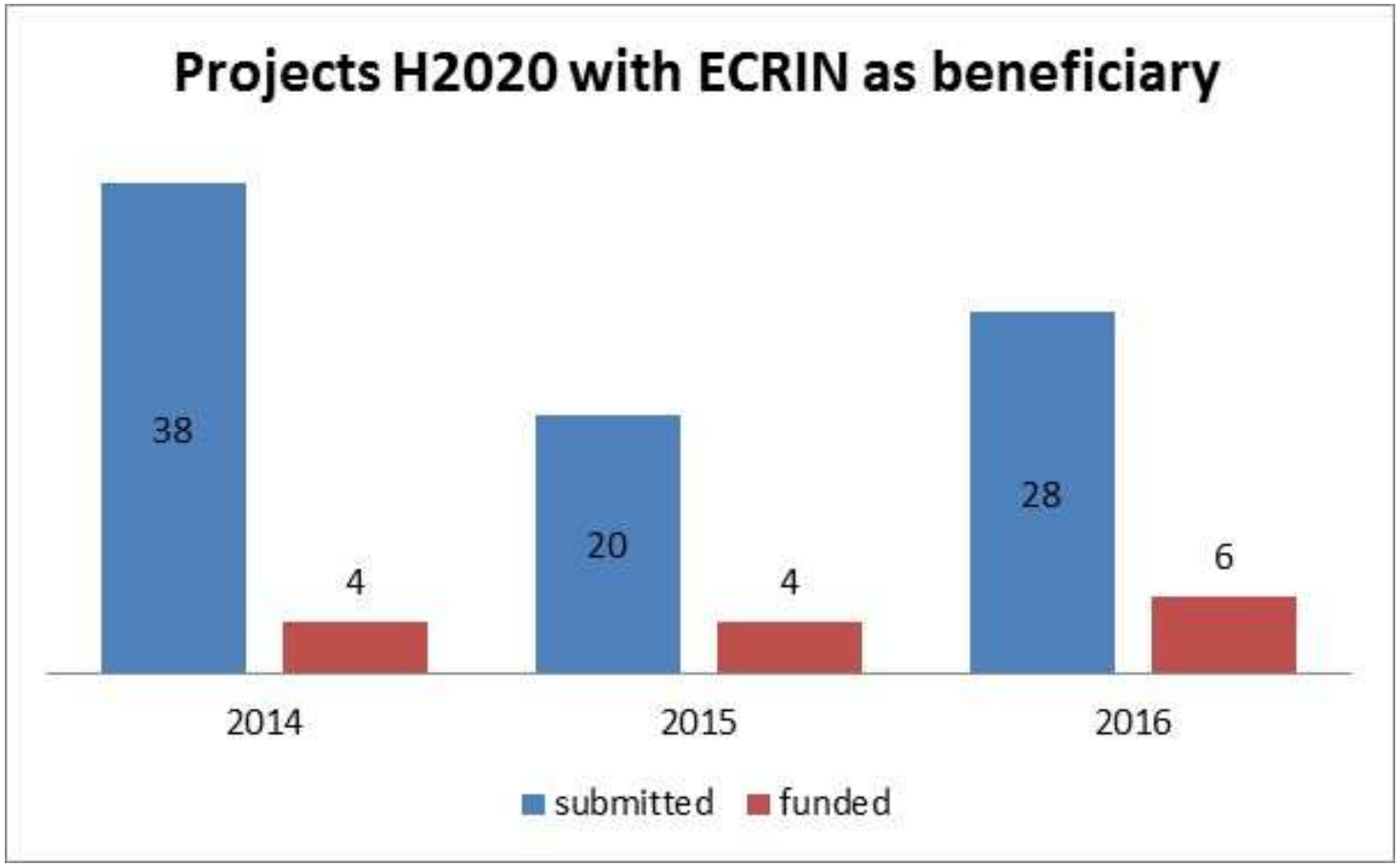
# ECRIN - Trial portfolio (10/2016)



# ECRIN – involvement H2020 proposals

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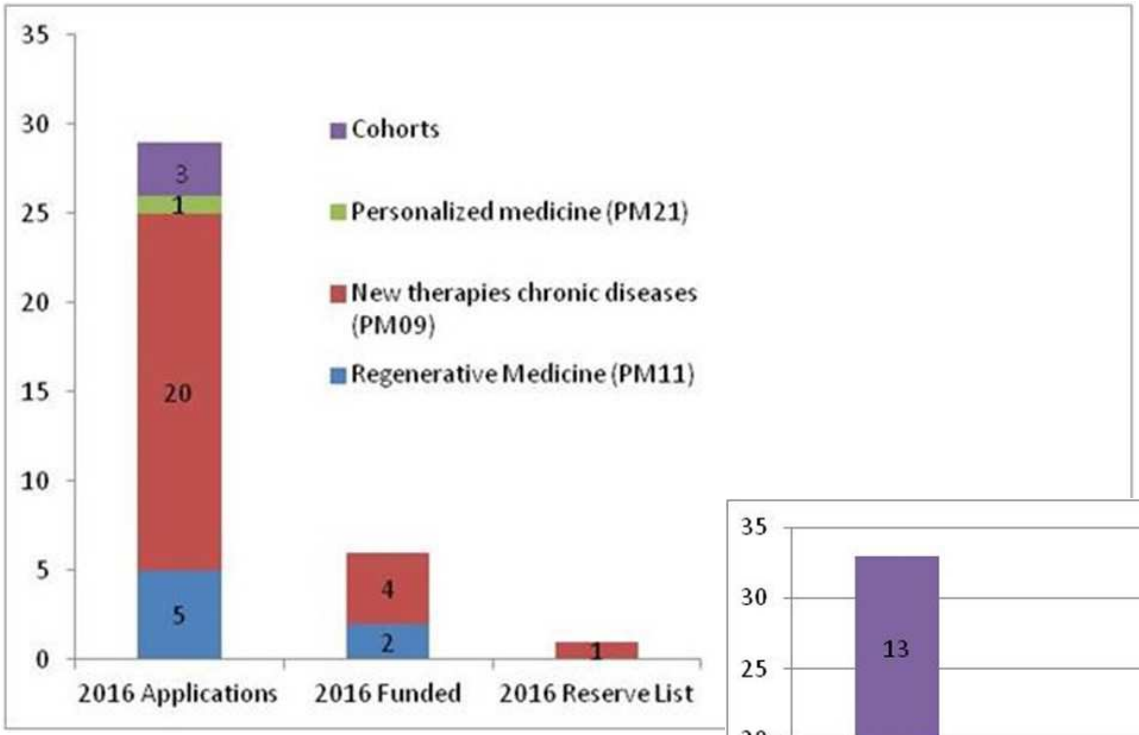
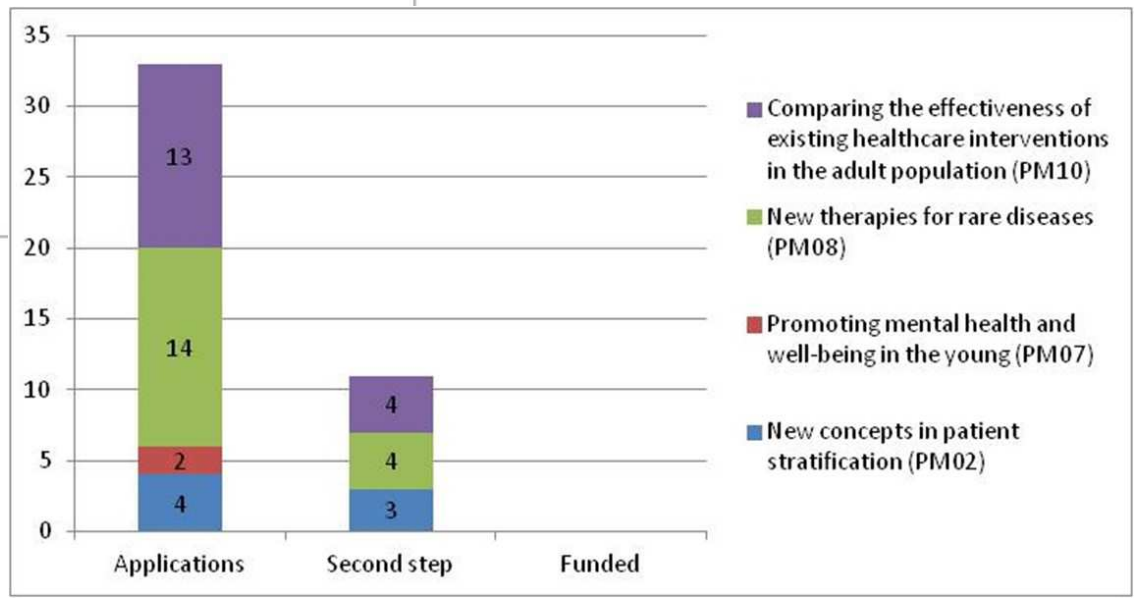
# ECRIN – involvement in 2016/2017 proposals

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# Budget calculation – for proposals

## preparation (1)

- **European Correspondent (EuCo) and/or ECRIN, Paris is contacted by sponsor/coordinator** - *sometimes late before deadline*
  - "support needed in preparing, starting and managing the clinical trial"
  - protocol - usually not available at this time (perhaps synopsis/clinical template)
  - list of participating sites - often preliminary (who is beneficiary?)
  - additional sites/country - often not known at this stage
- **EuCo will consult and**
  - inform how ECRIN is working with its EuCos and ECRIN partners
  - define which services could be provided and which responsibilities could be delegated from sponsor to ECRIN - *responsibility split*
  - suggest optimal structure - *experienced study team and lead CTU*

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# Budget calculation – for proposals

## preparation (2)

- **Discuss and collect information from sponsor/coordinator (approx. 2-4 weeks)**
  - input to synopsis-clinical template/ completion site list/ definition of number of patients per site/ type of study (drug/MD/both/other type of study)/definition of required services
  - contact study team (if available)/contact lead CTU (if defined)
  - summarize information and discuss/complete required services for all participating countries
  - Propose if needed management structure, organisation and “algorithms” for missing information and discuss with sponsor/lead CTU
  - Provide templates for responsibility split allocating tasks to all involved parties (later used as Annex to agreement sponsor/ECRIN)

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# Budget calculation – for proposals

## preparation (3)

- **Services usually requested are**
  - **Regulatory submission** to competent authorities (CA) and/or Ethics committtee(s) and follow-up (amendments etc.)
    - *Central activities (*for the whole study) performed by a lead CTU (mostly at the sponsor`s site),
      *national activities* performed by ECRIN partners in the participating countries
  - **Monitoring (**central/on site, local), including writing the monitoring manual, preparing/performing training (web-based), review of monitoring reports
  - **Pharmacovigilance** (central/local)
  - **Project management** (central/local)
  - **Data management** (central)

*could result in a work package " Management of the clinical trial " with ECRIN/lead CTU as WP lead*

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# Budget calculation – for proposals

## preparation (4)

- **Send out information in a structured format to EuCos in all participating countries asking for**
    - bottlenecks to be expected in submission, national requirements, …
    - cost calculation for different services defined
- EuCo in participating countries will **select/contact her/his national network/single CTU** (procedure defined by national network)
- Define **status of ECRIN partners within H2020 project**

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# Time frame

## Contractual issues (1)

- **site contract (sponsor/site)** - template/negotiation (feasibility/budget) *usual under sponsor responsibility*, *support by ECRIN possible*
  - relevant in addition to Consortium Agreement (CA)
  - defines tasks delegated by sponsor (AE/SAE reporting etc.)
  - may be required for EC submission (as template/with signature)
  - for some countries/sites bilingual and/or other local requirements (local template/quadripartite etc)

  *may take up to several months to be completed; follow up by ECRIN partner may accelerate (task to be considered in budget!)*
- **agreements ECRIN/sponsor** (with responsibility split and budget) – template available - *needs to be signed before below can be signed*
- **agreement ECRIN/ECRIN partners** (with responsibility split and budget) template available – *should be signed before first activity starts*

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# Critical points to be considered

- experience/sufficient capacity in sponsor`s team
- definition of central activities for the whole clinical trial to a lead CTU (project management, pharmacovigilance, monitoring, data management etc)
- knowledge of bottlenecks (type of study in the different countries, submission, specific requirements, contracting in all countries)
- awareness of responsibility of sponsor duties and relevance of delegation of tasks (specified in responsibility split with > 50 tasks) *example of responsibility split*
- consider realistic time lines for each activity - *with buffer*
- budget enough capacity/hours for single services *(budget!)*
- select patient recruiting sites based on *comprehensive* feasibility check

**Optimize procedures** *– templates for cost calculation, responsibility split, agreements, follow-up, feasibility check*

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# Crucial issues

## may influence budget and/or timeline

- Recruitment of patients
  - selection of sites – often without comprehensive feasibilty checks
  - discrepancy of inclusion/exclusion criteria and patient availability
- Drug availability
  - production (ATMP), storage, transport, distribution, dispensation, application
- Radiation permission (for Germany)
- Status of the study in the country
- Site selection (*national procurement rules/ link with existing beneficiaries*)

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# Crucial issues

- Comments from Evaluation summary reports (ESR) of EU proposals and that would be worth to consider
  - Sample size
  - Recruitment plan : recruitment too optimistic/period too short
  - Safety not enough addressed
  - Study monitoring (quality control) : underpowered/too low to ensure data integrity, rights and safety and well being of patients
  - Risk analysis
  - Others: Handling missing data/regulatory details to be adressed/gender issue/number of investigator

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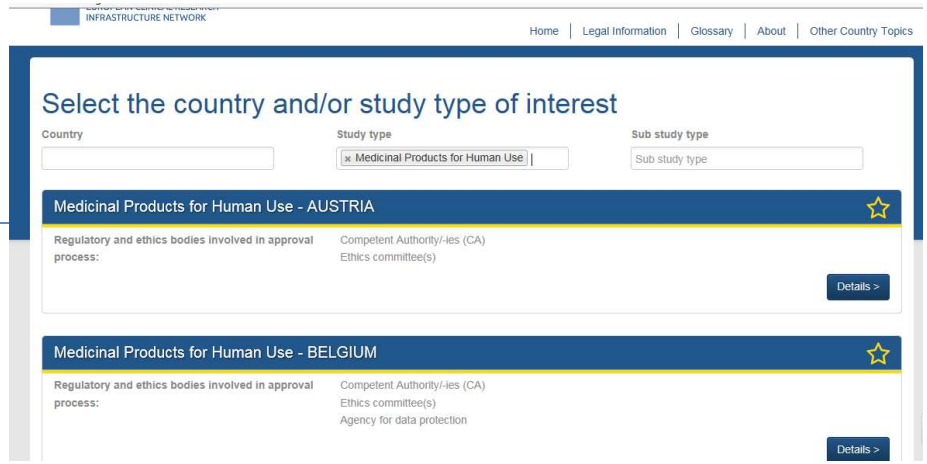
# ECRIN – useful tools




-ECRIN regulatory data base

(http://www.ecrin.org/tools/regulatory-ethical-tools)

For partners in projects

-Confidentiality agreement (CDA) – template

-Responsibility split – template with > 50 tasks listed

-Cost estimation – based on algorithms, template

-Agreement Sponsor/ECRIN – template

-Agreement ECRIN/ECRIN partners – template

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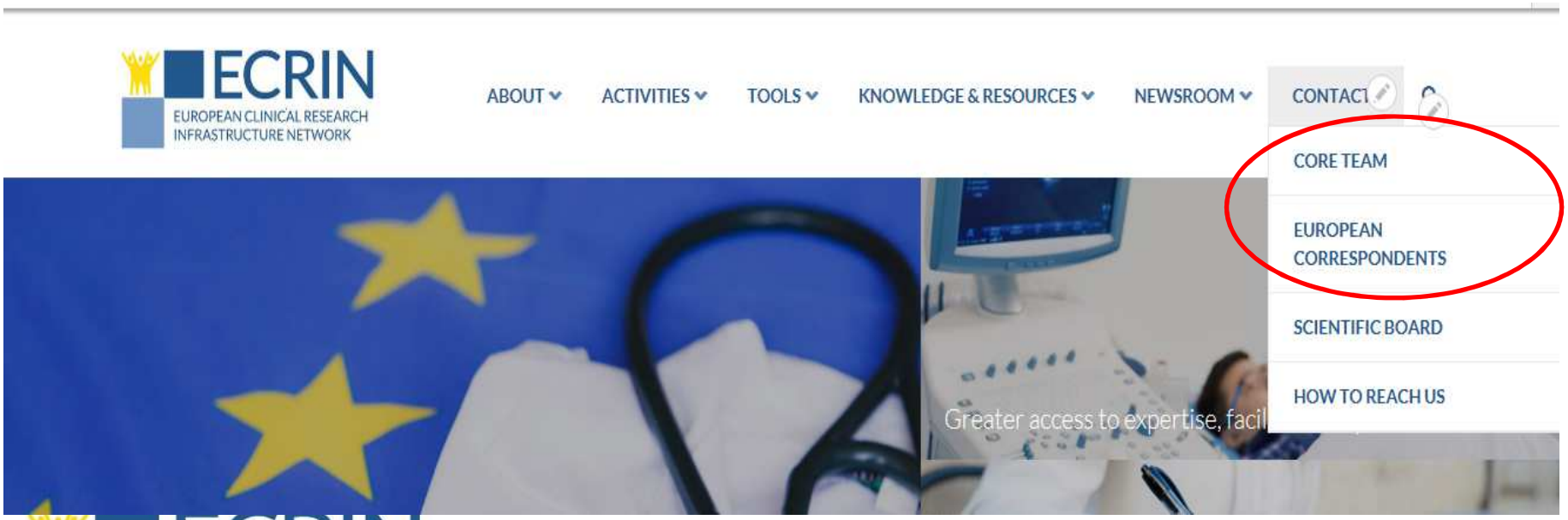
# ECRIN contacts

http://www.ecrin.org

-ECRIN European Correspondent in your country

-ECRIN core team



**Thank you!**

Any questions?

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