

CLL trials registry for improvement in the long-term follow-up of CLL patients in European Trials: an ERIC Initiative

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Need of a CLL Clinical Trials Registry

Long-term FU is needed because of:

- Data on OS needed → the most important end-point!
- Data on response to relapse treatment needed
- Development of resistant genotypes (i.e. p53 deletion)
- Data on secondary diseases (neoplasia, cardiac disease, etc. needed to avoid another VIOXX)
- Indications that the EMEA may demand long-term FU

Problems with long-term FU (IITs and company-sponsored trials) :

- Extremely expensive to keep a trial open
- Enthusiasm wanes as Investigators move onto next trial
- No further FU after primary endpoint was met
- Results of after initial publication are rarely reported

Concept of the CLL Clinical Trials Registry

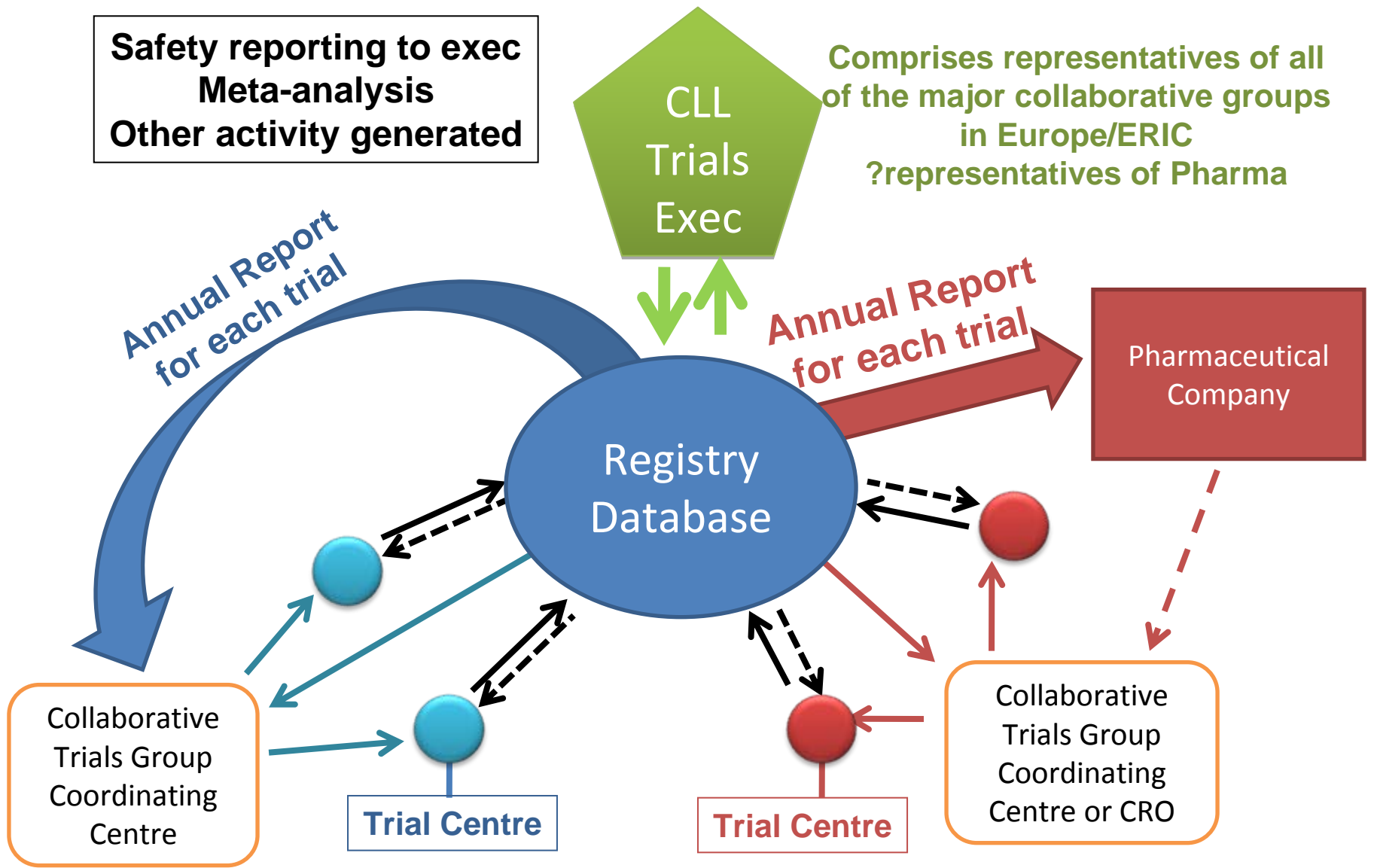
Purpose of registry:

- Offering long-term FU service
- Allowing wider analysis including meta-analysis and assessment of responses to subsequent treatments

Concept:

- Web-based system with simple Registry data annually
- National register/ co-ordinating centre
- Executive Committee drawn from European Trial groups
- Registry needs to be a “stand alone” NGO (non-government organisation) → contracts, legal standing, etc.
- ERIC is the parent organisation

Structure of the CLL Clinical Trials Registry



Data collection

- Primarily web-based, but paper is also possible.
- Language: primarily english with categorical lists in different languages.
- Time point of register:
 - When primary endpoint was reached (for company initiated trials)
 - From randomization
- Data transfer of original trial database including a minimal data set defined by the IWCLL:
Diagnosis, stage, age , Risk factors, treatment regimen, response, PFS.....

Ethics and Regulatory Issues

- Ethical approval for standard patient registration and consent form
- Patient consent form
 - at entry into original trial
 - at time point of entering the registry
- Contract between Registry and study group/Commercial partner re: use of data
 - In principle data still reported by the original organisation
 - For use of non-owned data application to the executive committee is necessary.

Problems to overcome

- Complex ethical issues
- Complex regulatory issues
- Setting up the Registry in multiple countries
- Governance of Registry
- Maintaining confidence of participant organizations
 - Collaborative groups
 - pharmaceutical industry
 - Regulatory authorities
 - Ethics committees

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- Need an experienced Registry company



Clinical Research



ICON Clinical Research Lifecycle Sciences Group (LSG)

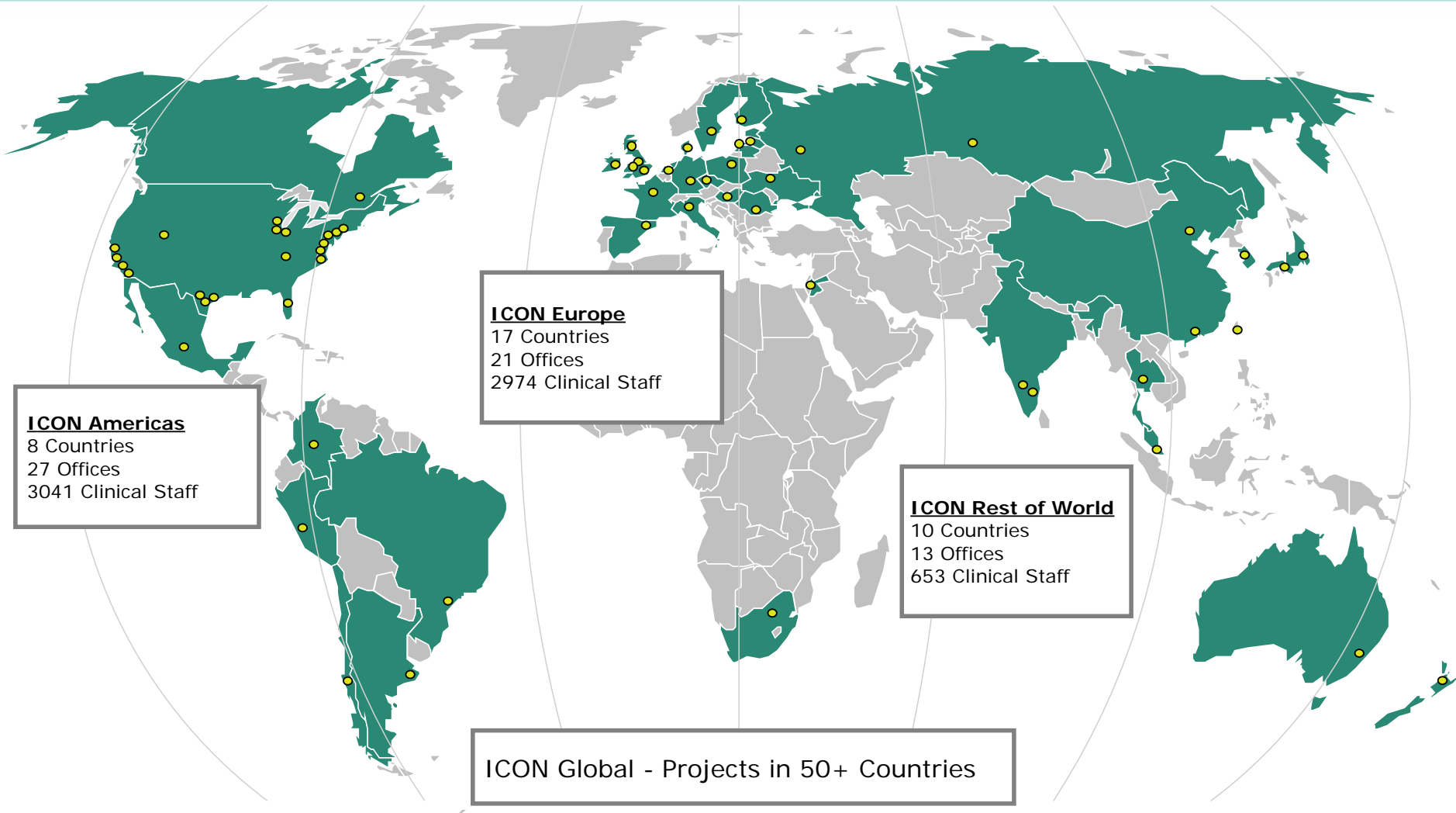
Registry Capabilities
06 December 2009

- **Functional Experience**
 - Over 12 years' experience in pharmaceutical / biotech industry
 - 10 years' experience in observational research design and implementation, post-marketing safety surveillance
 - Experience in country-specific and global programs
- **Therapeutic Experience**
 - Experience across all major therapeutic areas including hematology, gastroenterology, pulmonology, and pain management
- **Other Relevant Experience**
 - Member, ISPOR Pt Registry Design & Operations Working Group
 - Numerous publications and presentations in field of observational research

- **Global Full Service CRO**
 - European CRO, headquartered in Dublin, Ireland
 - Organic Growth & Strategic Acquisitions
 - > 7,000 staff in 71 offices in 38 countries worldwide
 - 2008 Revenue = \$865 M
 - 90% repeat business
- **Global commitment to quality**
 - ISO9001 (2000) accredited
 - Global SOPs
- **ICON Differentiators**
 - Simple reporting lines within Project Teams
 - ‘Hands-on’ Senior Management Involvement / Governance
 - EDC Expertise
 - LSG’s Registry Experience

Global Reach

71 Locations; 38 Countries



ICON Oncology Experience - Past 5 Years

Phase	No. of Studies	No. of Patients	No. of Sites
I	41	1054	117
II	72	7944	1571
III	50	25139	3540
IV	3	928	54
CLINICAL TOTAL	166	35065	5282
Consulting	43	NA	NA
Biometrics	92	5658	463
Imaging	127	8048	1595
IVRS	136	47169	7305
Other	32	2108	250
TOTAL	596	98048	14895

Scientific Expertise

- Health Economics and Outcomes Research
- Epidemiology
- Observational Studies
- Phase IV and Large Simple Trials
- Statistical Analysis
- Scientific and Medical Communications

Operational Expertise

- Study Start-up
- Site Management
- Data Management
- Statistical Programming
- Project Management
- Management of Scientific Advisory Boards

- Strategy & design throughout product lifecycle
- Scientific Advisory Board coordination
- Regulatory requirements & considerations
- Communication & publication plan(s)
- Analytic plan
- Safety reporting & surveillance approach
- Recruiting & retention approaches
- Data collection platform

- **Study Start-up**
 - Executive Committee meeting
 - Define strategic objectives
 - Materials development
 - Protocol
 - ICF template
 - Physician agreement
 - eCRF specs
 - Study reference binder
 - Data collection system development
 - Web-based system
- **Site recruitment**
 - Execute site contract
 - Local IRB support (as necessary)
 - Training

