How European Biological and Medical Sciences Research Infrastructures boost Innovation by Open Access

EU-OPENSCREEN's impact on innovation

Dr. Katja Herzog

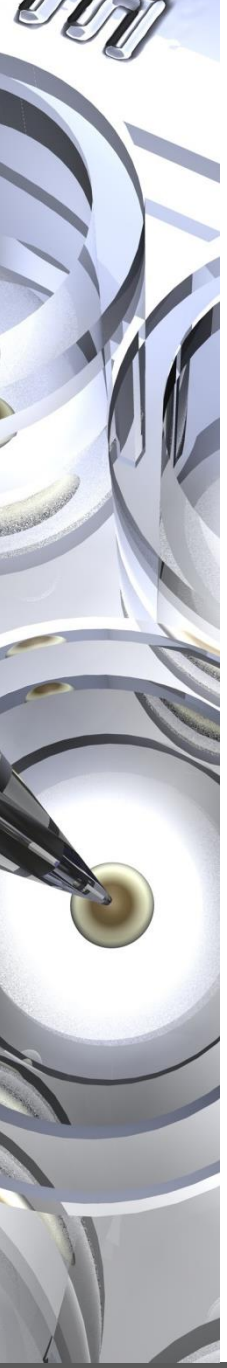
20.6.17

Brussels

What is innovation?

What is innovation?

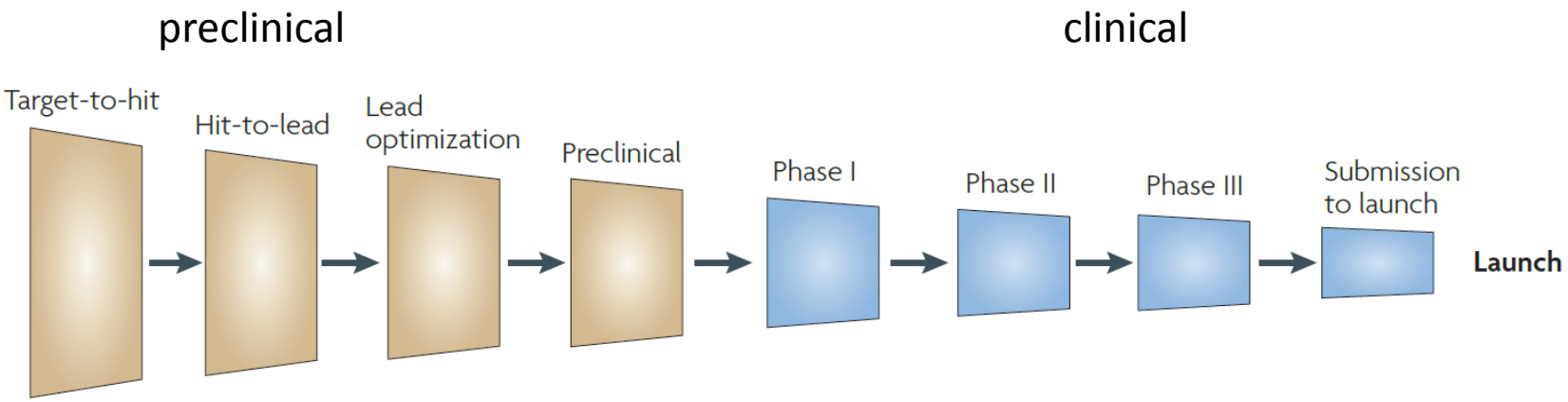
INNOVATION = real problem + creativity + action



INNOVATION = real problem + creativity + action

in biomedical sciences

THE PROBLEM:
High attrition rates are an ongoing challenge in drug discovery



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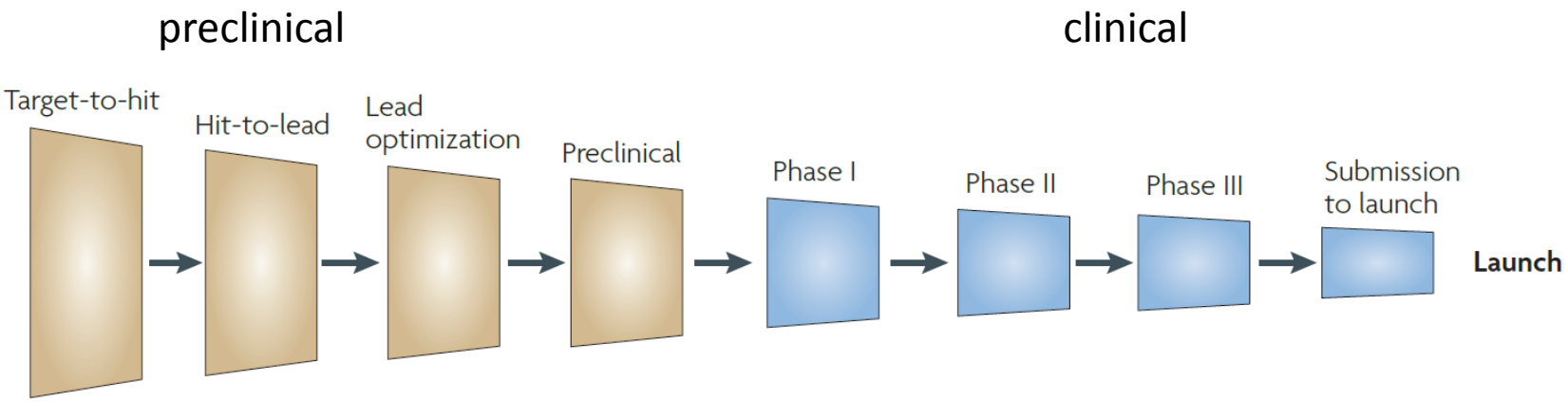
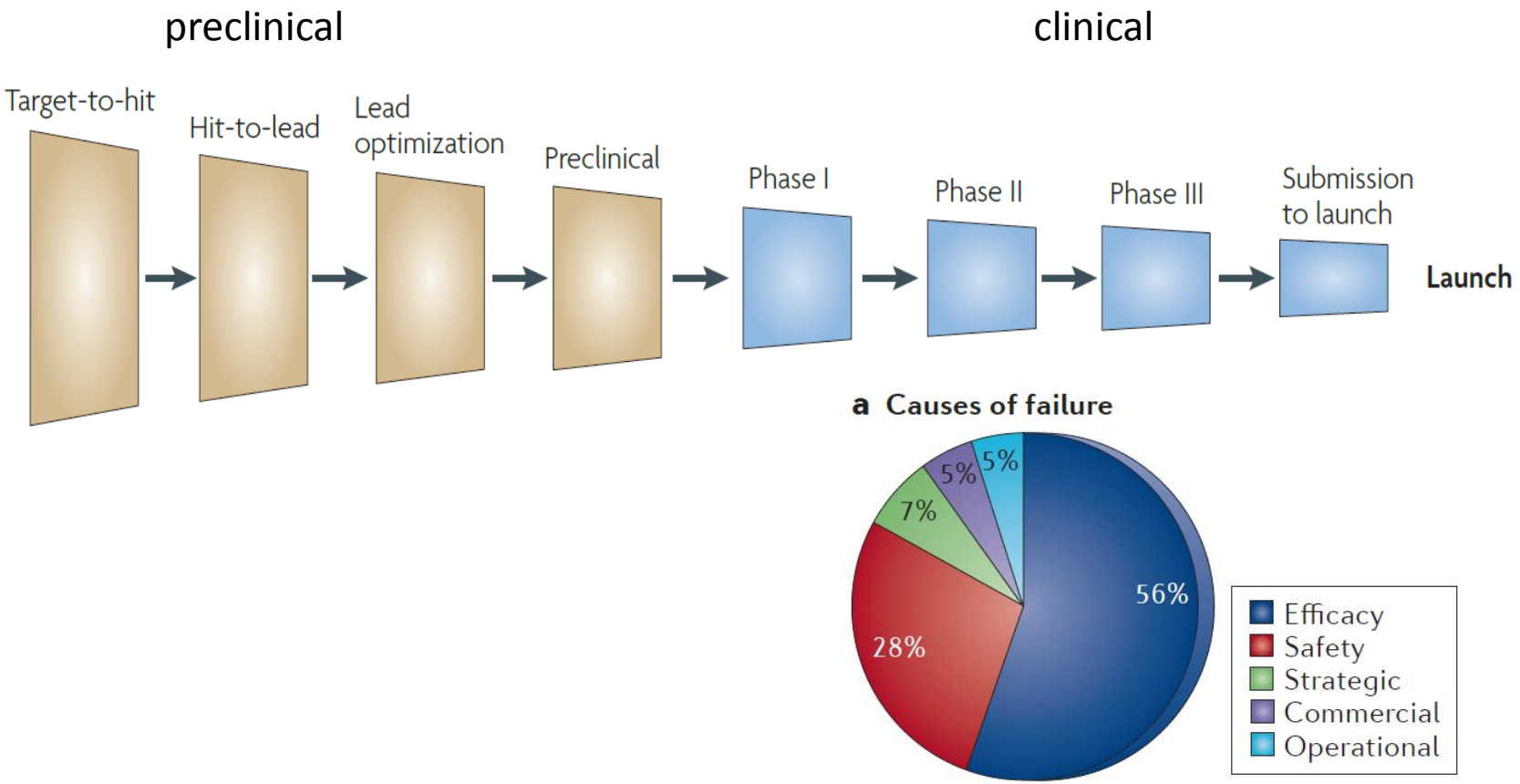


1) For which reasons do clinical trials fail?

2) What are innovative ways of improving clinical trial success rates?

Paul et al., 2010, Nat. Rev. Drug Discovery

Causes of clinical trial failure



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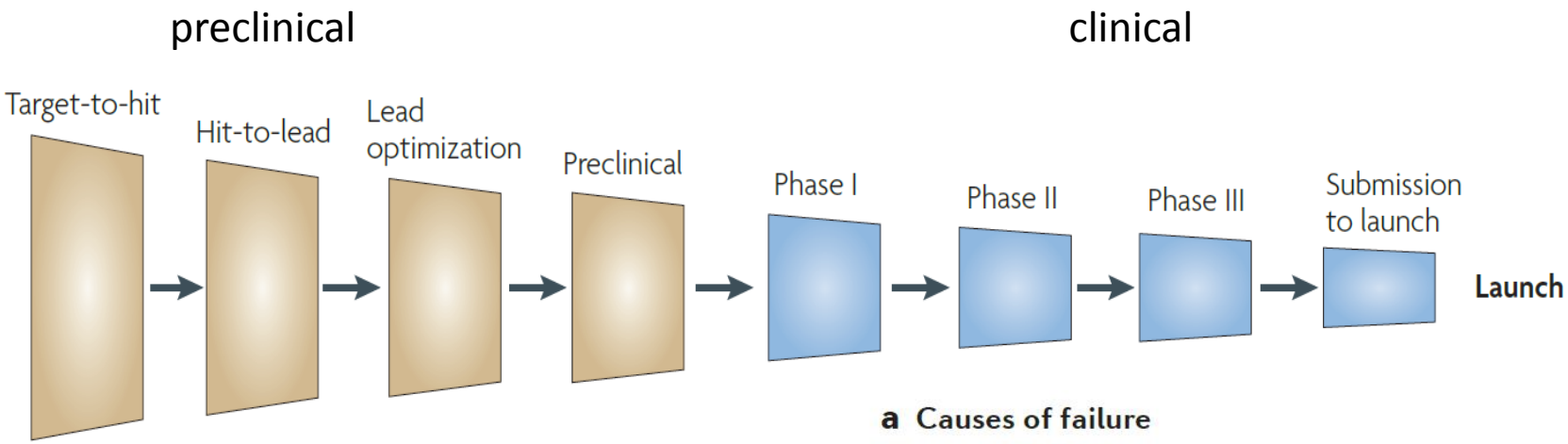
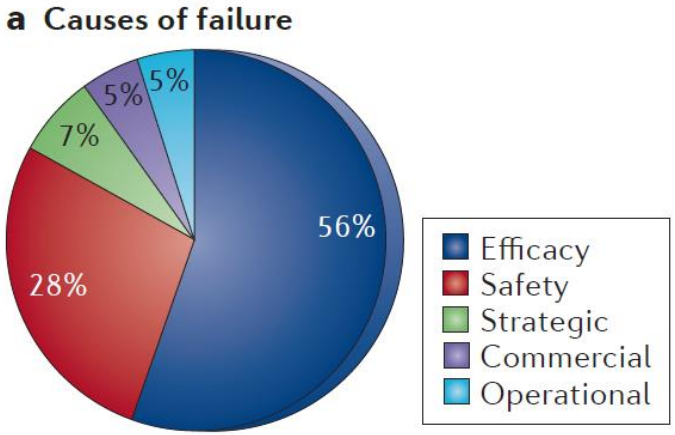


How can we increase the efficacy of drugs?



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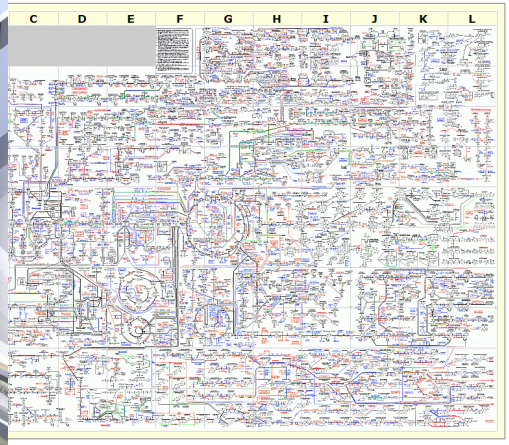


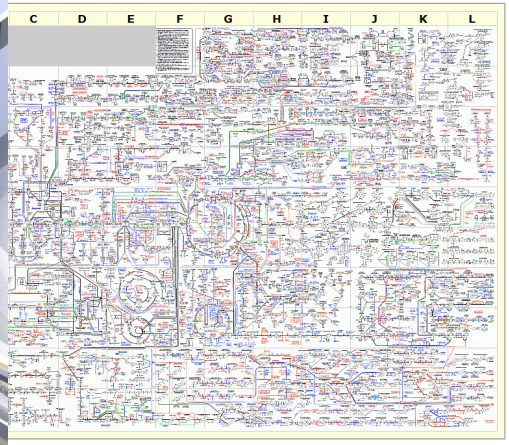
Self-evident:

- Better defining molecular mechanisms underlying biological processes

How can we better define these molecular mechanisms?

- by studying the effects of compounds on biological systems to gain insights into cellular or organismal metabolic or signaling pathways (e.g. implicated in the progression of diseases)

How can we improve the efficacy of drugs?



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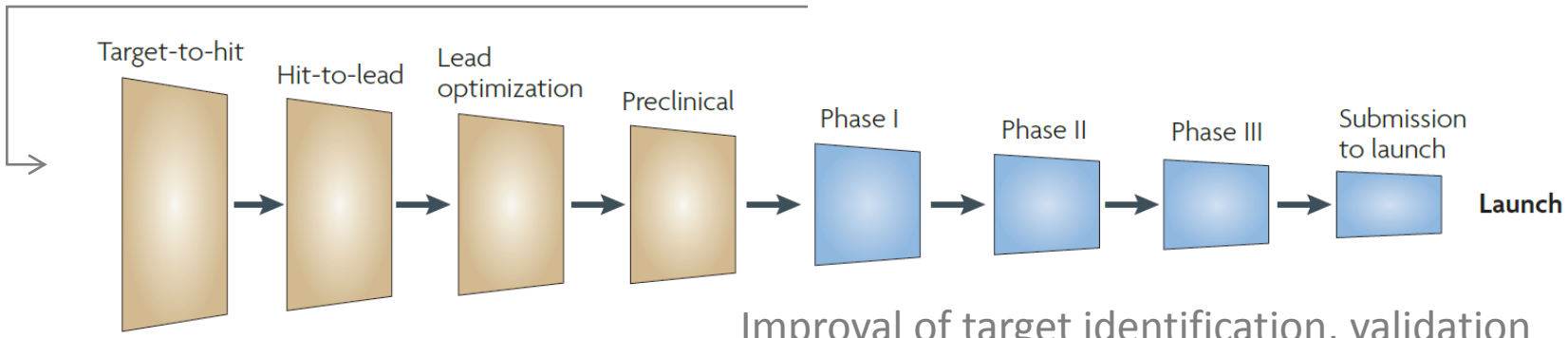

Improval of target identification, validation

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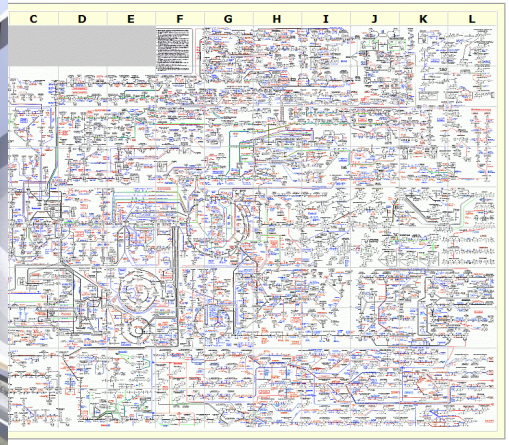

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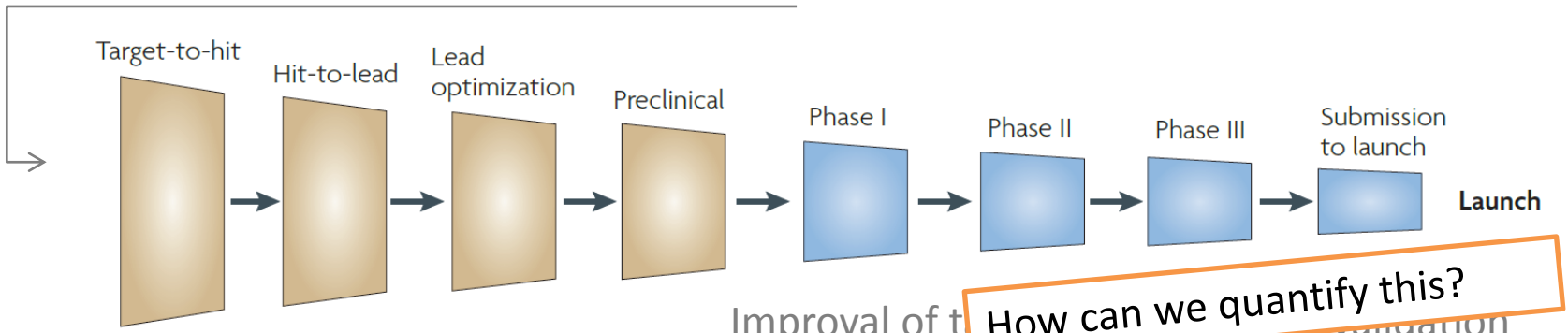

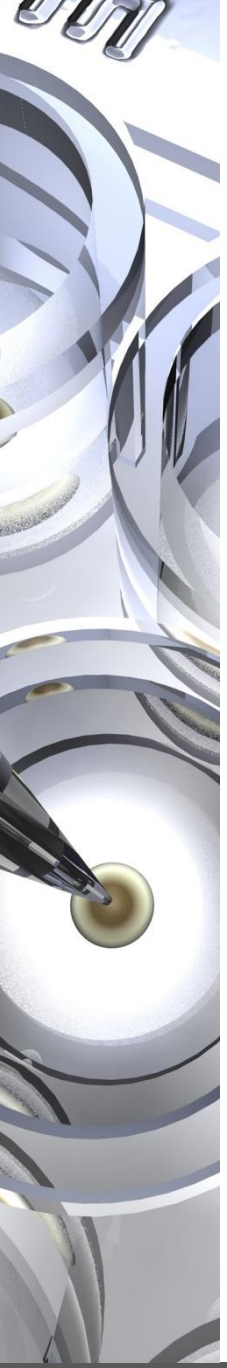

INNOVATION = real problem + creativity + action

THE CREATIVITY:
Modelling attrition scenarios

Phase	Cost	Success rate	number of project	portfolio cost
Target to Hit	1	80%	64	64
Hit to Lead	2,5	75%	51	129
Lead to candidate	10	85%	39	386
Candidate to FTIH	5	69%	33	164
Phase I	15	54%	23	339
Phase II	40	18%	12	488
Phase III	150	50%	2	330
Launch	40	91%	1	44
Market	264		1	1943


How to improve R&D productivity: the pharmaceutical industry's grand challenge

Steven M. Paul, Daniel S. Mytelka, Christopher T. Dunwiddie, Charles C. Persinger, Bernard H. Munos, Stacy R. Lindborg and Aaron L. Schacht

Data from Paul et al., 2010, Nat. Rev. Drug Discovery
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Economic model of drug discovery & development:

- P= [(WIP)x p(TS) x V] / [CT x C]

- Elements with highest impact?
- Improval of high-impact elements?
- Magnitude of improval?

P= R&D productivity

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Increase in success rate of phase II trials through increase of number of early drug discovery (e.g. target validation) projects

What happens to the overall cost of one drug reaching the market?

Data from Paul et al., 2010, Nat. Rev. Drug Discovery
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Even though the number of projects is increased at an earlier phase of drug discovery, the costs of one drug reaching the market could still be decreased by 30%.

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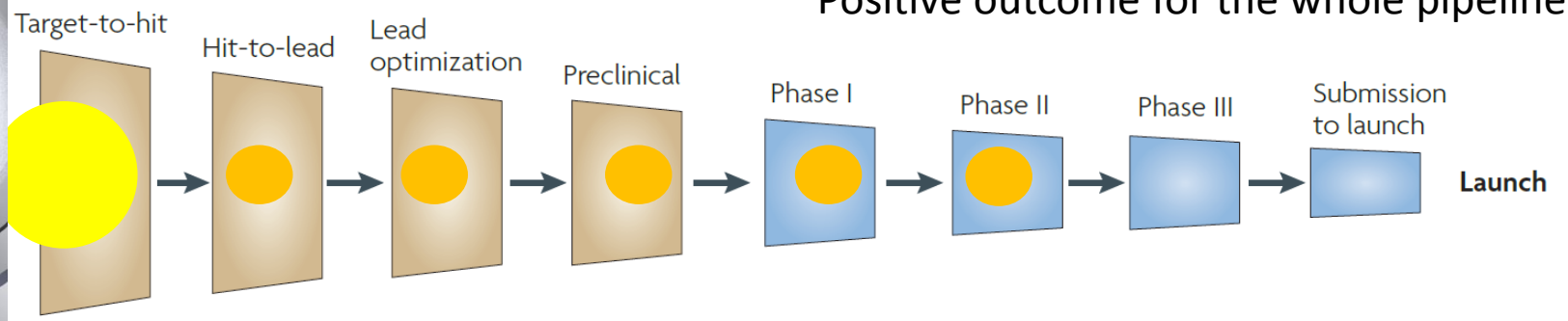
Positive outcome for the whole pipeline.



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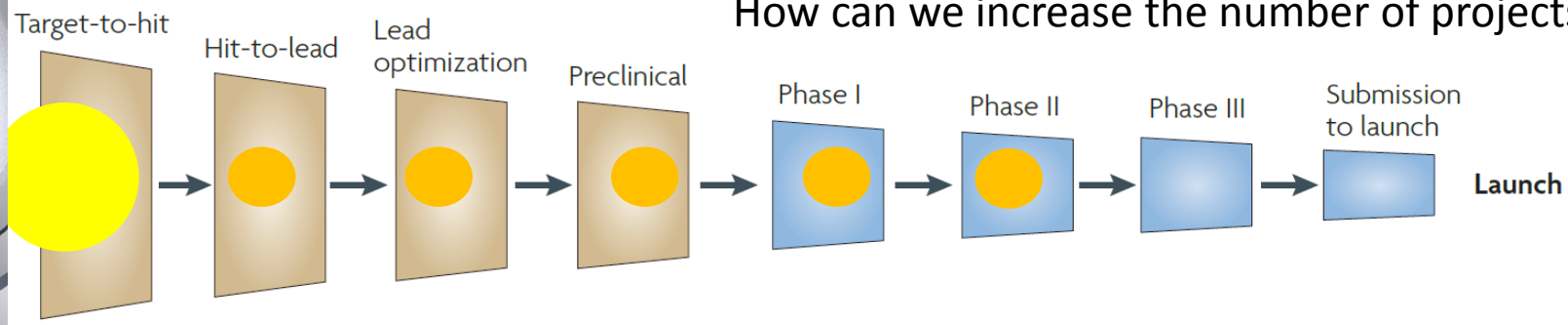

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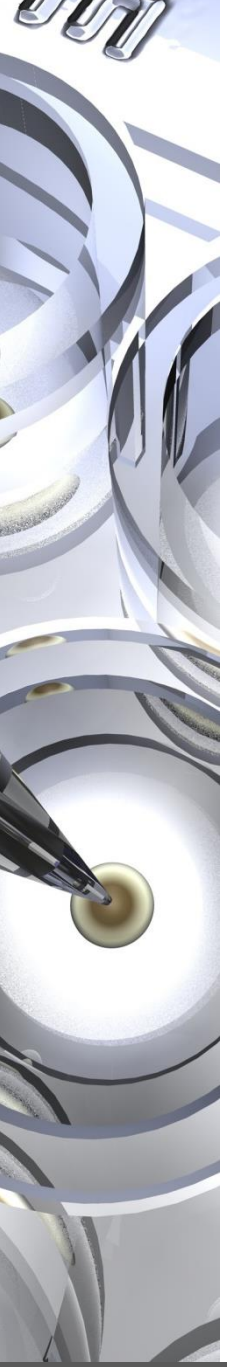
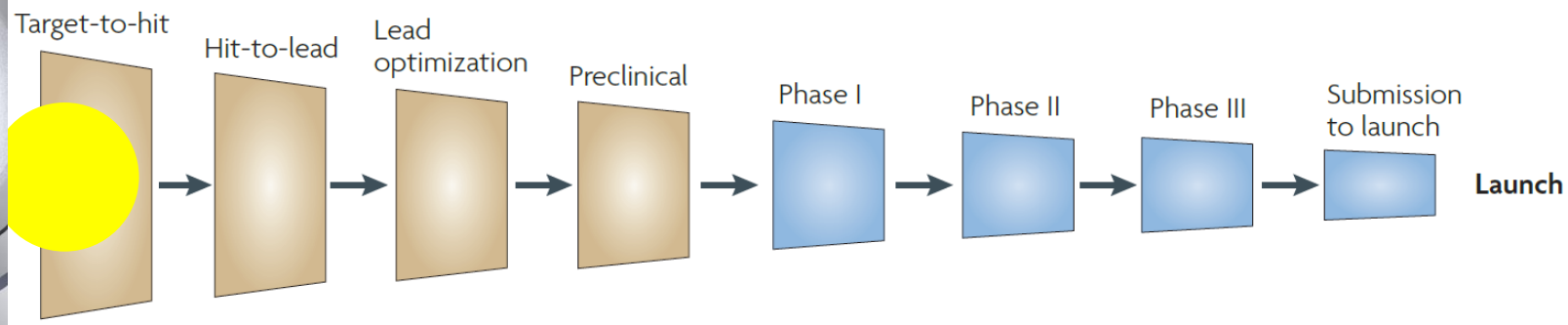


INNOVATION = real problem + creativity + action

THE ACTION:
EU-OPENSCREEN and early drug discovery/ chemical tool development



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THE ACTION:
EU-OPENSCREEN and early drug discovery/ chemical tool development

- Facilitates the access to
  - Systemic screening of a large quality-controlled compound collection with dedicated bioassays
  - Assay adaption
  - Medicinal chemistry for hit optimisation

EU-OPENSCREEN‘s impact on innovation in a nutshell

Open access through EU-OPENSCREEN

↓

Increased number of early drug discovery projects

↓

Better understanding of cellular/molecular processes

↓

Increased success rates for clinical trials

↓

new medicines

Additional measures to impact on innovation

- through network of partner sites: development of operating/technical standards= increase in quality
- through inclusion of southern/eastern european research communities: discover unvalidated targets, new ideas around more established targets

- open access to generated research results through open database without any restrictions on use of data → maximum dissemination and exploitation of data
- database will be linked to existing life science databases (ChEMBL) and informatic resources

- engage and work with SME's and Industry to bridge the innovation gap and facilitate collaboration between Industry, Users and Partner sites (Berlin Partner & Pharma Solutions network Berlin – locally)

Thank you for your attention. Any questions?

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How can R&D productivity (P) be increased?

Economic model of drug discovery & development:

- P= [(WIP)x p(TS) x V] / [CT x C]

- Elements are interdependent

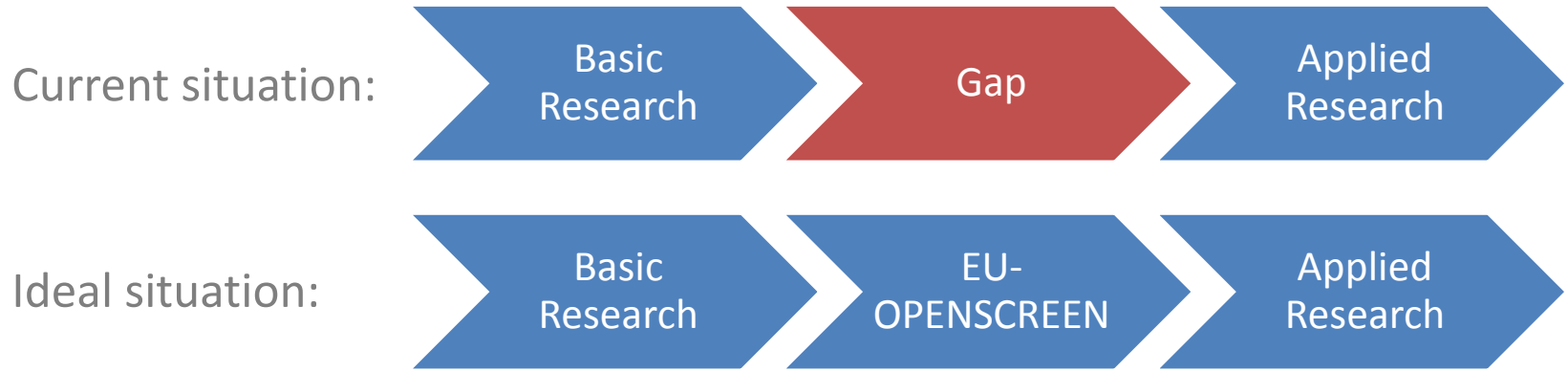
- Elements with highest impact?
- Improval of high-impact elements?
- Magnitude of improval?

EU-OPENSCREEN tries to improve the current research landscape as a response to ongoing challenges

Identification of active compounds is expensive and highly demanding in resources and know-how

Requirements exceed capacities of many institutes and even countries

Coordination of required resources is necessary across borders



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Setup of EU-OPENSCREEN

Headquarters (FMP, Germany):

Centralized:

- Compound management
- Bioprofiling
- Database
- Project management

- Newly generated data
- Locally collected academic compounds

- Copy of compound collection and regular library updates
- Forwarding of project requests to suitable partner sites
- Bioprofiling data for submitted academic compounds
- Access to database
- Common operating standards

Partner Sites (member countries):

Distributed:

- Screening
- Medicinal chemistry
- Assay adaptation

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Benefits for local scientific communities: EU-OPENSCREEN impact on innovation

Local EU-OPENSCREEN Partner Site

Partner Site is visible within EU-OPENSCREEN network and will thus attract new international users who are interested in expertise present at the partner site.

Chemist (local or external) (compound provider)

By submitting their compounds, Chemists can expose their molecules to a wide variety of biological assays present within the EU-OPENSCREEN network.

Biologist (local or external) (assay provider)

Biologists can screen the EU-OPENSCREEN library at the partner site and identify new tool compounds/ gain insights into molecular pathways.

Data User

Deposited data can be accessed freely to supplement ongoing or design new experiments (e.g., **ChEMBL**): academia + industry!

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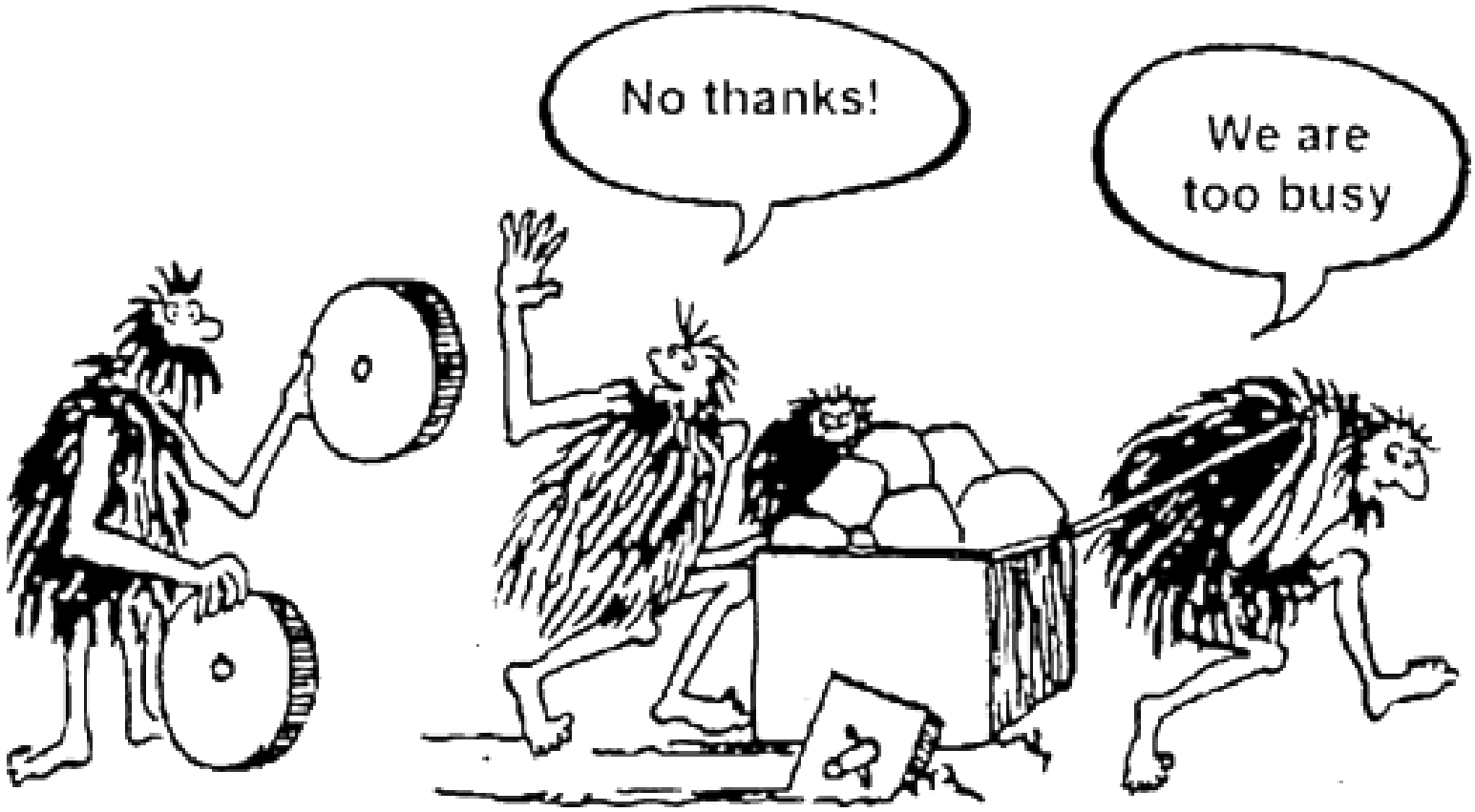

No thanks!
We are too busy

Position paper: data management

→ data management and sharing among European Research infrastructures (Blomberg et al., 2014)

February 5, 2014

Working paper | Open Access

Principles of data management and sharing at European Research Infrastructures

ELIXIR; EU-OPENSCREEN; BBMRI; EATRIS; ECRIN; INFRAFRONTIER; INSTRUCT; ERINHA; EMBRC; Euro-BioImaging; LifeWatch; AnaEE; ISBE; MIRRI; Blomberg, Niklas (editor); Meiners, Torsten (editor); Suhr, Stephanie (editor)

Key Performance Indicators (KPIs)

- = monitor and evaluate impact of RI
- SMART principle
- Significant, determinable
- Progress in attaining the KLP will be reviewed by Steering committee every three months, and by AOM every 12 months
- KPIs with regards to its three major user groups
- 1) assay providers
- 2) compound providers
- 3) database users

Table with KPIs

Key Performance Indicator (per year)	2018	Scalability	2021
Number of users accessing the screening infrastructure	30		50
Number users accessing the database	>1,000		>10,000
Number of tool or lead compounds developed (1 per screening project)	0		50
Number of scientific publications that result from experimental work at RI (at least 1 peer reviewed paper submitted per project as part of the deliverables for project acceptance, with open access journal publication strongly preferred)	0		50
Number of patents (expected for 5-10% of projects)	0		2-3
Number of chemists donating compounds	200		200

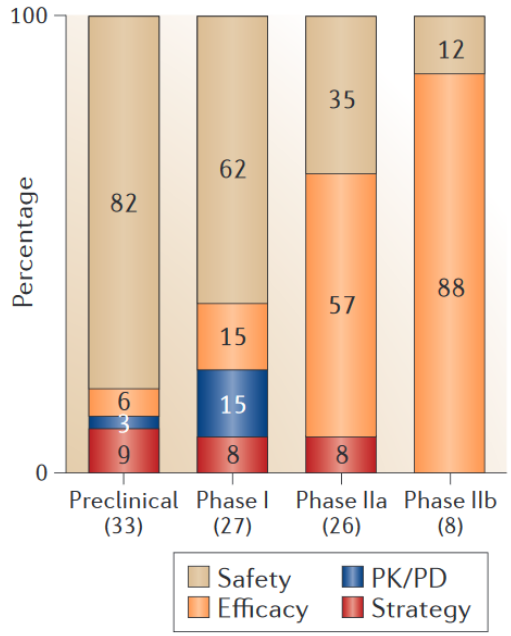
Ensuring impact, novelty and scientific excellence

- **Excellence-driven access**: It is anticipated that the great majority of Assay Providing User projects will enter under an excellence-driven process. Here, Assay Providing Users will already have received a positive readout from an external competitive grant review (e.g. Horizon 2020, ERC, National funding programmes and internal institutional innovation schemes) leading to the securing of funds for project execution. It is EU-OPENSCREEN ERIC's position that this upstream peer-review process will have established the underlying quality of the User's project in terms of scientific excellence, novelty and impact

- 2015, external consultancy (WK Life Sciences Ltd) analysed positioning of EU-OPENSCREEN and our prospective number of screening projects
- *All of the open innovation Pharma initiatives [in the European Union] have commercial potential at their heart and [certain] proposals are selected by a committee heavily biased towards pharmaceutical industry demands. One can therefore predict a demand from established European screening communities for access to screening facilities in respect of targets* ***considered uninteresting by Pharma.*** *This demand would include the search for tool compounds or probes to elucidate target biology as well as potential drugs per se. Further, there is a large* ***scientific community within the European Union, primarily in the southern and eastern countries within Europe, who have no practical access to screening facilities whatsoever, who*** *will seek access to EU-OPENSCREEN facilities in respect of unvalidated targets and potentially also for novel ideas around more established targets. Because of its willingness to address unvalidated targets, and scope extending beyond human health to animal health and crop protection, EU-OPENSCREEN will be complimentary rather than competitive with commercial screening platforms, and other EU-funded initiatives, as it will feed those same platforms with new targets and probes to enable target validation. Although some overlap with existing initiatives might be anticipated the scope and focus of EU- OPENSCREEN means that the demand for slots would, largely, be in addition to the screening activities already available.*

Ongoing challenge in drug discovery

High attrition rates:



Cook et al., Nat. Rev. Drug Discov., 2014

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Infrastructures to support excellent research

"Modern research in all scientific fields requires **expensive instruments** and **resources**, and is characterised by a continuous interplay between new scientific challenges and our technical responses to them."

(European Strategy Forum on Research Infrastructures)

Physics | Astronomy | Biological & Medical Sciences | Social Sciences | Information Technology

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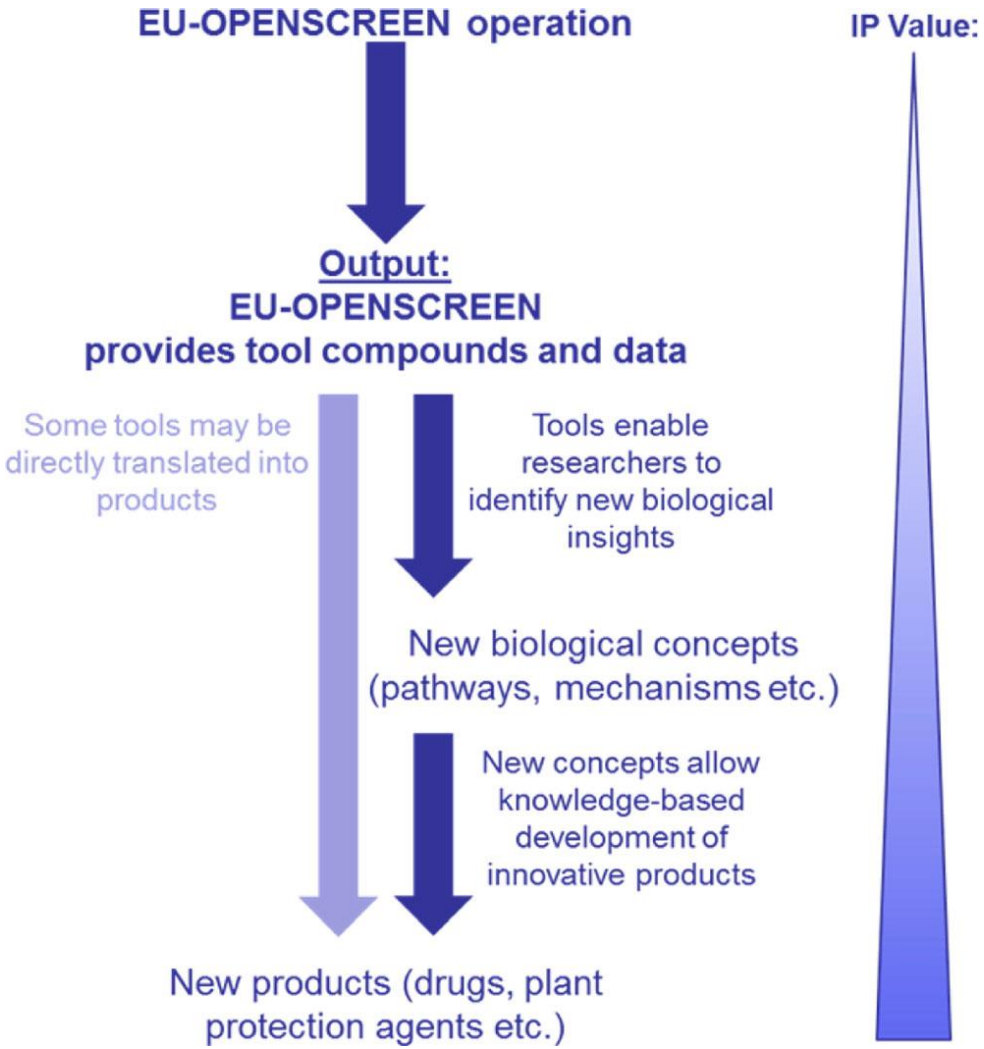
Facilitated access for european researchers

- Majority of scientist in europe: no access to technology platforms + compound collections required for devleopment of tool compounds
- Construction of jointly used compound collection
- Operation of open-access database accessible on a global basis

- GAP PICTURE (southern/eastern research communities: un-validated targets, new ideas around more established targets)


EU-OPENSCREEN operation
IP Value:
Output:
EU-OPENSCREEN
provides tool compounds and data
Some tools may be directly translated into products
Tools enable researchers to identify new biological insights
New biological concepts (pathways, mechanisms etc.)
New concepts allow knowledge-based development of innovative products
New products (drugs, plant protection agents etc.)

Benefits EU-OPENSCREEN

- Build central, jointly-used, quality-controlled bioprofiled compound collection/ compound management with relevant chemical diversity
- Distribute collection among partner sites
- Support outstandning projects by channeling through the central hub to most appropriete site with required expertise
- Make publically available all generated tools and data through central database
- Development of operational standards,
- Enabling of cross-experiment data analysis
- For chemists: activity definition through user assays

EU-OPENSCREEN support

- Assay development
- Screening
- Follow-up chemical optimisation
- Biological validation

- Will implement an open-access policy to encourage maximal data dissemination and publication (same rules for academia and industry) (optional 18-month embargo period to withold data to allow for the translation of research results)
- → position paper on data management and sharing among European Research infrastructures (Blomberg et al., 2014)

February 5, 2014

Working paper | Open Access

Principles of data management and sharing at European Research Infrastructures

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- Straightforward integration of data in other chemical resources on the internet
- ChEMBL: structure-activity relationships (SARs)
- PubChem: chemical structures
- UniProt: targets

Pharma solutions network Berlin (Berlin Partner)

- engage and work with SME’s and Industry to bridge the innovation gap and facilitate collaboration between Industry, Users and Partner sites

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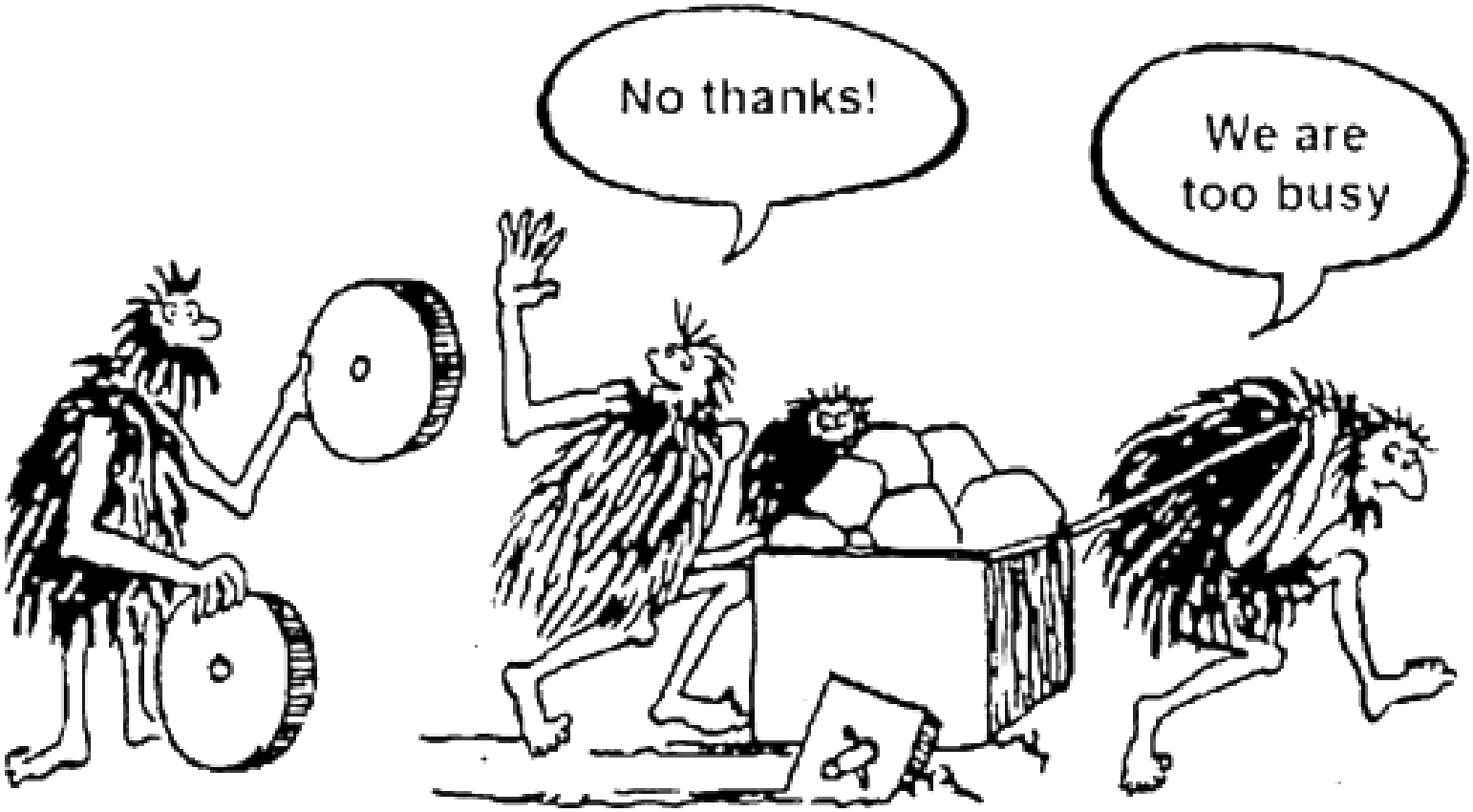
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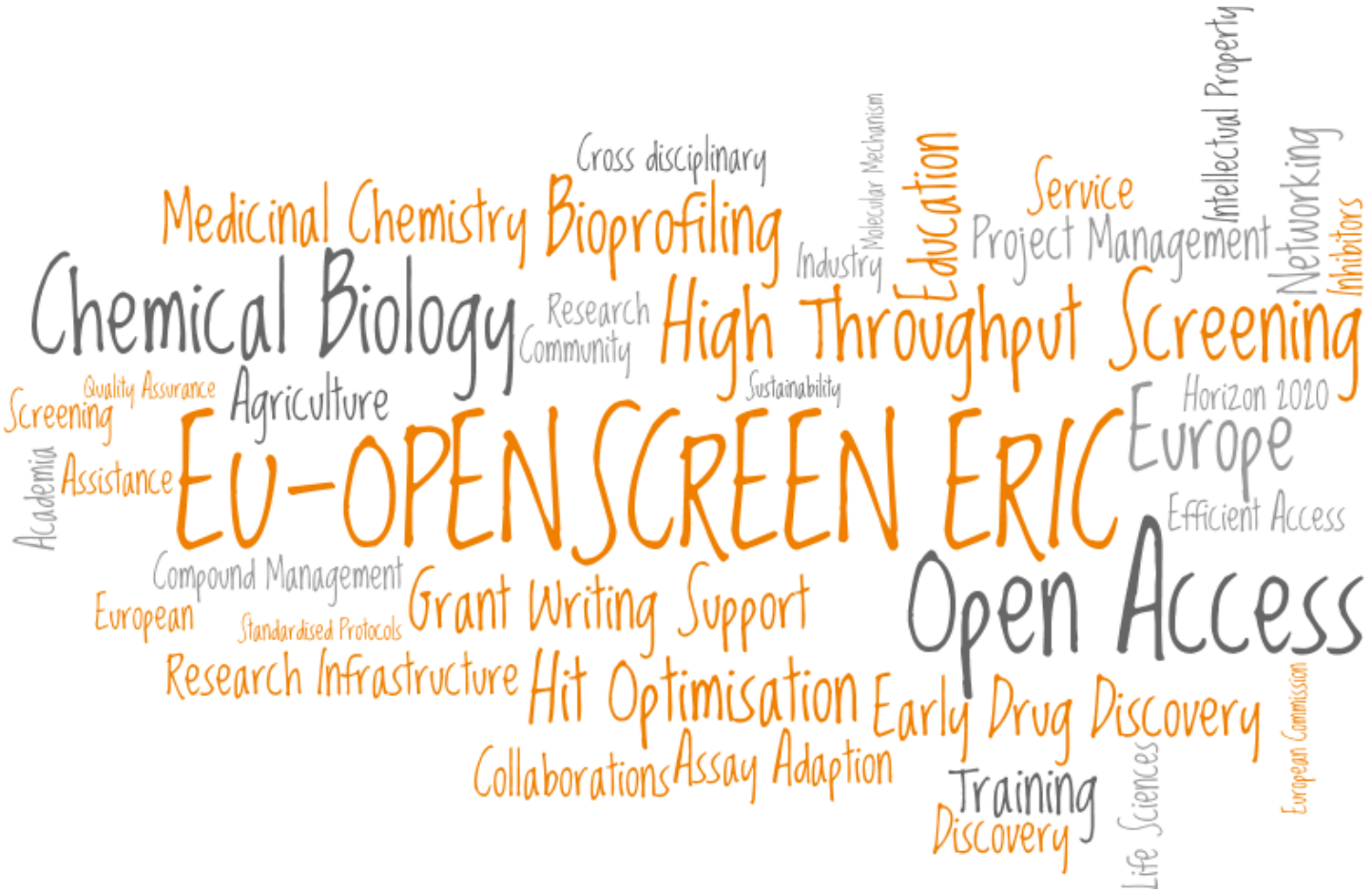
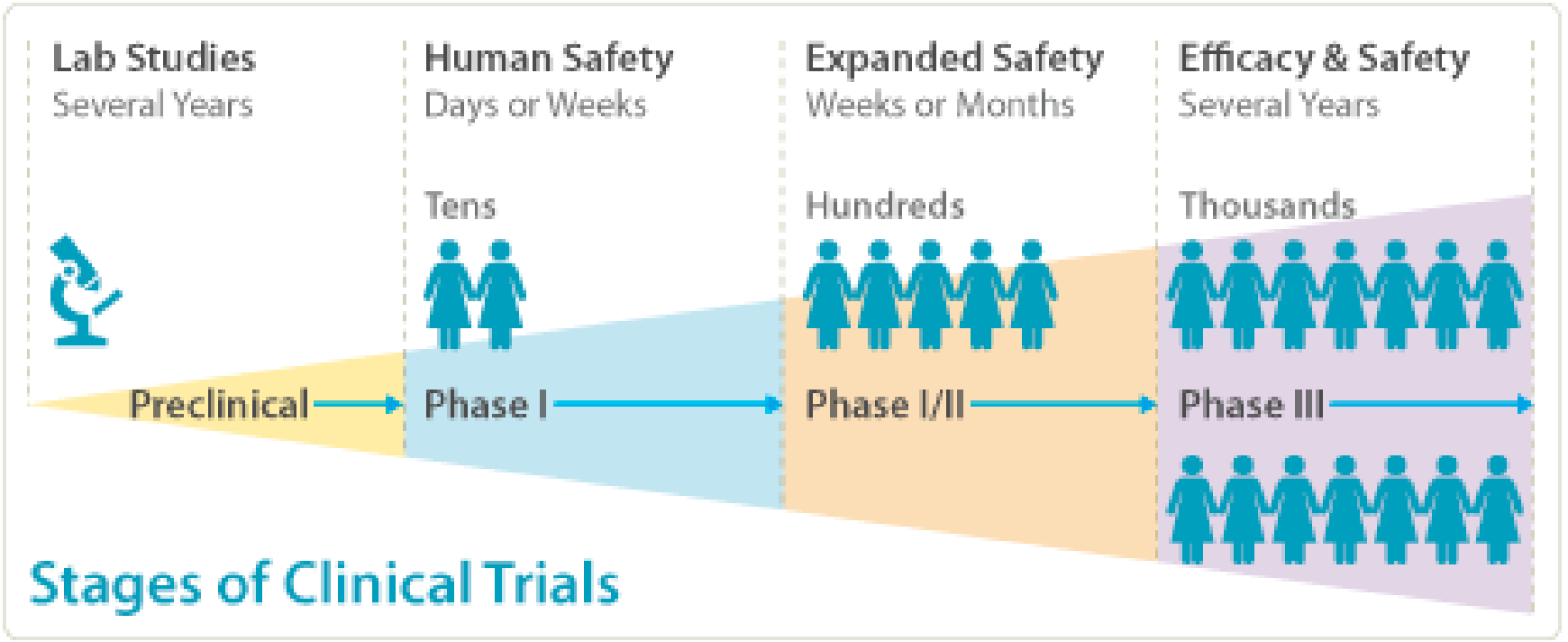
We are too busy

Thank you for your attention. Any questions?



eu openscreen



https://www.ipmglobal.org/our-work/research/clinical-trial/clinical-trials-approach