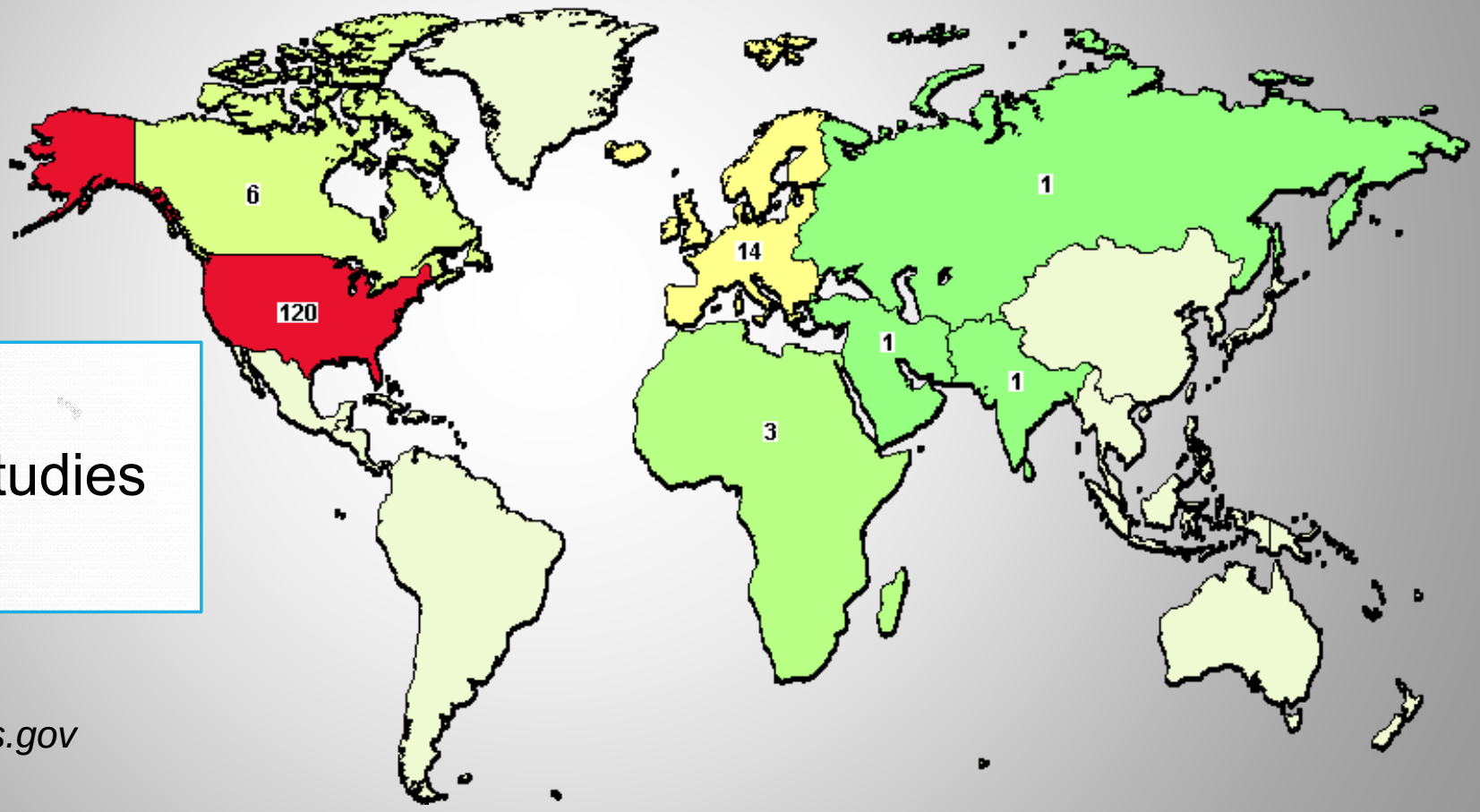
THE IMPORTANCE OF CLINICAL RESEARCH CENTER RIGHT SELECTION

TO DEMONSTRATE THE RELIABLE SAFETY DATA OF NICOTINE CONTAINING PRODUCTS

Some facts:

- despite general acceptance that smoking is harmful, a substantial number of adults continue to smoke
- the development of potential reduced exposure products has been suggested as a way to reduce the risks of tobacco smoking
- valid human clinical trial is critical to determining the risks and/or benefits from these products
- the most important is: the safety of subject and reliability of delivered data

Recruiting Studies | nicotine



146 studies

Source: *clinicaltrials.gov*
June 6th, 2018

RESEARCH CENTER

How to find the right Research Center?

What expertise should the Center possess?

Are there any regulations regarding Centers?

Regulations regarding Centers:

- there are no regulations for research centers, however, they are for centers of clinical research
- Clinical Research Centers should be taken into account when Sponsor places the study of tobacco products, due to:
  - standardization of the process,
  - the vast experience in conducting complicated studies in terms of the large number of procedures in short time

Recommendations regarding the requirements for Clinical Research Centers

- European Medicine Agency
  - EMEA/CHMP/SWP/28367/2007- http://www.ema.europa.eu
- The Association of the British Pharmaceuticals Industry
  - Guidelines for phase 1 clinical trials – http://www.abpi.org.uk

High requirements for the staff of the Center

- experienced team:
  - general training
  - training dedicated to the study protocol
  - permanent training in emergency procedures (basic / advanced)

STUDY SPECIFIC MOCK TRAINING

(the feasibility of the procedure over time)

subject's path
the way of the tested product
sample route

Case studies

Case 1:

Day	Time (h) (post-dose)	Real Time (h)	PK sampling	Blood for Safety	Urine Sample	ECG, HR, BP	Other
1	predose	x	x	x	x	x	
3	30	02.00	x			X	
3	42	14.00	x			X	
5	**84**	**08.00**	**x**	**x**	**x**	**x**	**Breakfast at unit; Physical Exam incl. Skin Exam**

Case 2:

For the first visit, where the patient needs to stay overnight, to minimize disruption to the patient the catheter must be attached to a **1.5m long line with 3-way stopcock** at the end so that patient does not need to be woken or interrupted when **taking blood**.

Quality management system

- standard operating procedures (SOP)
- audits and internal controls regarding processes and documentation
- supervising the implementation of audit recommendations
- external controls of subcontractors
- training in the regulations regarding clinical trials, SOP and GCP principles

Quality system

The sponsor is ultimately responsible for the quality and the integrity of the trial data. However, all the units should have their own system, such as ISO 9001, for quality control and quality assurance, which the staff must follow.

Guidelines for Phase 1 Clinical Trials, abpi 2012

Specific tobacco study related issues:

- there is no any regulation or legislation that prevents you from performing smoking/vaping events as required (e.g. indoor smoking ban)
- Center should has:
  - access to the smokers population
  - experience in conducting studies evaluating tobacco products
  - experience in human smoking topography measurements
  - experience in spirometry measurements

Smoking area

- there should be significant number of dedicated smoking areas for all arms of smokers.
- smoking areas should be:
  - within the premises of the clinic
  - or the passageway from the clinic to the smoking areas should be monitored and supervised by the study personnel.

Ethics Committee issues

- from our previous experience, there were no general objections to the aim of the studies
- some ethical issues were related to the question if study procedures and requirements for subjects wouldn't encourage them to smoke more cigarettes
- all the studies must obtain the Ethics Committee's approval

What are your key points to ensure that study performed at selected Center delivers the reliable safety data of nicotine containing products?

- close communication with the sponsor
- QA procedures properly planned and performed
- well trained, experienced staff
- good organization - detailed plan of study activity prepared per study staff and per study subjects
- large data base of ready – available subjects
- experience of the site in 24 hours urine collection
- appropriate equipment to curry out the study procedures
- possessing risk management policy

Experience in smoking studies

Type of project	Number of subjects	On-site / out-patient
Evaluation the exposure to selected smoke constituents in smokers	40	On-site (8 days)
Comparing the levels of biomarkers of exposure in smokers	128	On-site (8 days)
Evaluating the changes in biomarkers of cardio-vascular risk	320	Out-patient (1-month)

Start up time:
About 2 weeks from SIV to First Subject In

THANK YOU FOR YOUR ATTENTION!

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