Industry Perspective On Clinical Trial Environment In China
产业对于我国临床试验环境的总体认知

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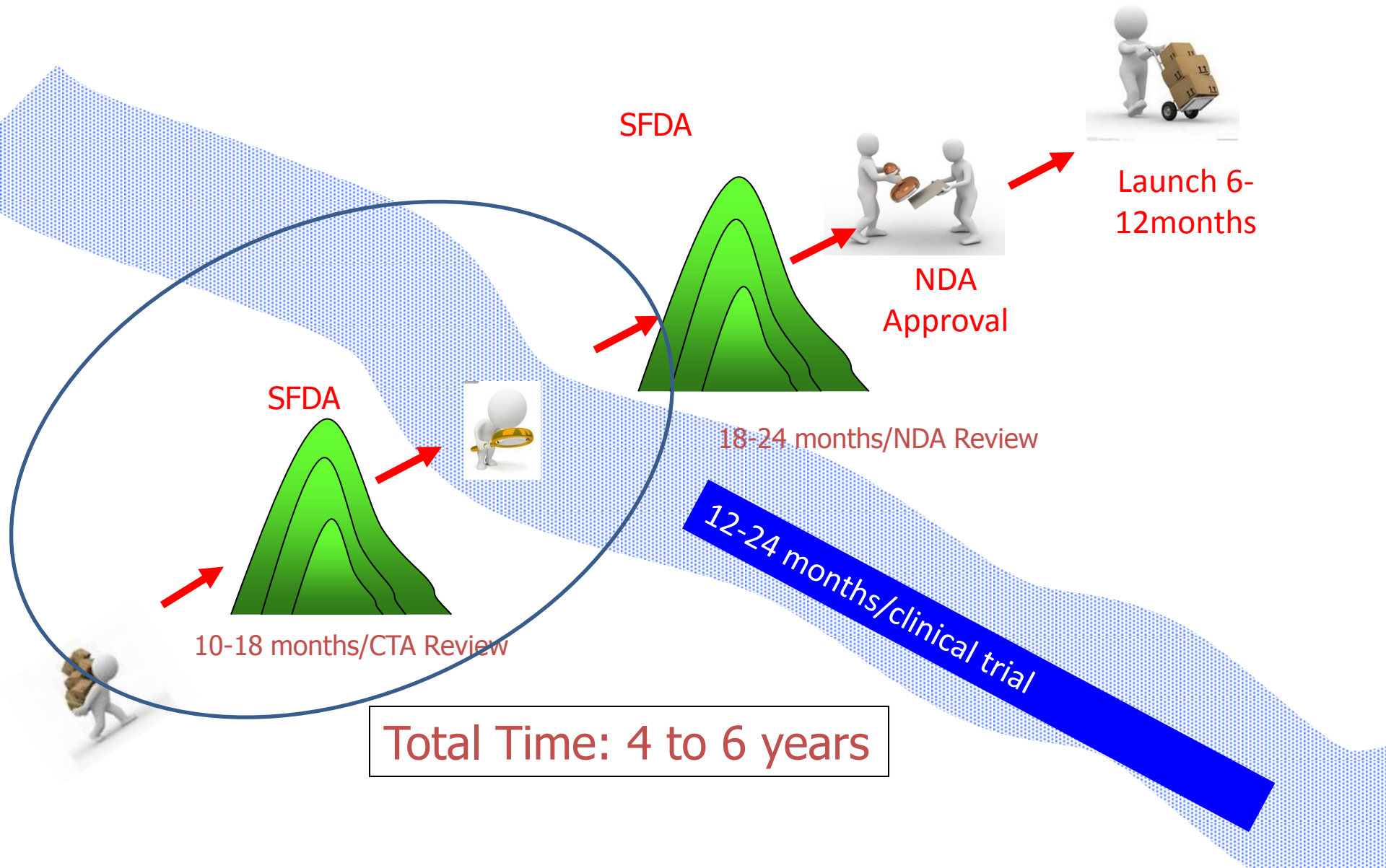
Topics 主要内容

- Clinical Trial Requirement in China
  临床试验的总体要求
- Pathways For Clinical Trial Initiative
  申请临床试验的通道
- Clinical Trial Execution
  临床试验的开展

Clinical Trial Requirement In China
临床试验的总体要求

Drug Registration in China



Clinical Trial Requirement In China
临床试验的总体要求

- Independent Development/独立开发的药品（Cate I/II 药品）
  - Phase I/II/III/IV (I/II/III/IV期临床试验)
  - Need statistical significance for Ph III (三期临床试验需要统计显著性设计）

- Bridging Development /桥接开发（Cate III/IV/V 药品）
  - PK+ validation study（100 pairs)
  - Randomized control design & No mandatory significance request，随机对照设计，无强制统计学要求
  - Surrogate endpoint can be applied per global ph III data 基于已有的全球数据，可考虑替代终点等简化设计

Some Problems In Clinical Requirement/临床试验要求存在的问题

- Minimal pts number in Ph I/II/III
  I/II/III期临床的病例数的简单化规定
- No clear guidance for most TA, eg total patient exposure, endpoint selection, disease model
  针对多数治疗领域，没有明确的临床指导原则，例如患者总暴露，临床终点选择，疾病种类等
- Inconsistent practice in statistical requirement for Cate III drug 对于三类药的统计学要求不一致
- Not separate bio-originate and biosimilar in Cate VII
  生物制品7类不区分原创药品和生物相似物药品的临床要求
- Even skip PK for cate XV (bio-generic/similar)
  生物相似物15类不要一期试验,直接上III期

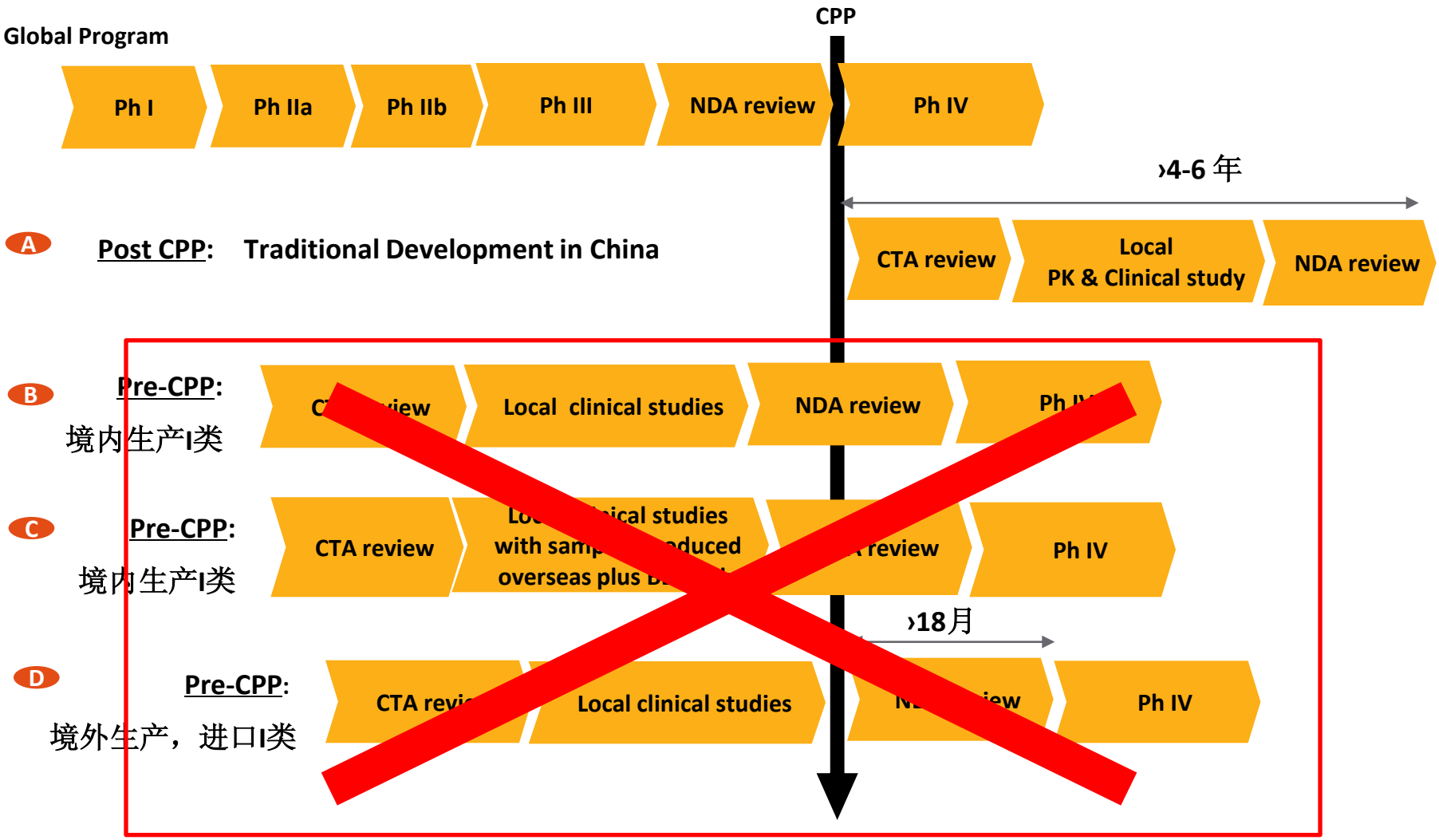
- Simplified requirement for scientific issue 复杂问题简单化
- Complicated requirement for simple issue 简单问题复杂化

Pathways For Clinical Trial Initiative
申请临床试验的通道

Pathways For Clinical Trial Initiative
申请临床试验的通道

- Traditional Registration Study CTA
  注册临床试验
- Global/Regional Study CTA
  国际/区域多中心
- EAP/NPP/Compassionate Use
  患者早期/同情用药计划

Traditional Registration Study CTA
注册临床试验
(中国单独开发产品路径)



Global/Regional Study CTA
国际/区域多中心（1）

- Pivotal studies参加全球主试验
  - Pros优点：
    - Join simultaneous development 与全球研发完全同步
    - Avoid duplicated investment重复投入少
  - Cons缺点：
    - Most pivotal studies missed due to Lengthy review
      目前CTA 的时限导致失去大量机会
    - Variations/amendment in CMC/protocol not supported under current law frame
      研发过程中的变更得不到法规支持
    - Chinese patient number cap in pivotal study 中国患者的人数达不到未来NDA的要求（CTA时限/患者比例控制）
    - No guidance to link global study to China NDA
      NDA指导原则不明确

Global/Regional Study CTA
国际/区域多中心（2）

- Regional studies参加区域性试验
  - Pros 优点：
    - Less variation in CMC/protocol
      方案和药学变更少
    - Sufficient Chinese patient data in regional study , esp study led by China
      以亚太为主导的数据量，尤其中国人的数据量充足
  - Cons 缺点：
    - Not preferred by some reviewers
      目前被一些审评人员和部门诟病其目的和意图
    - Lag behind global pivotal study
      比主试验的进程滞后

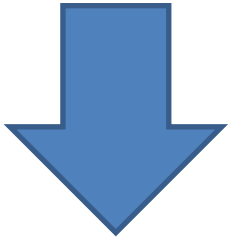
EAP/NPP/Compassionate Use
患者早期/同情给药计划

- No clear regulation or guidance support EAP/NPP/Compassionate Use

  目前没有明确的患者早期/同情用药计划的法规

  - Hospital apply for the use and approved by SFDA
    医院出面向SFDA申请，并获得批准
  - Has to be filed as CTA with a protocol which take one yr
    设计成临床试验申请，用一年多时间申请
  - Applied per individual patient base without SFDA endorsement
    按照病人个人用药实施，避开监管

Difficulties in CTA Pathways 进退两难的窘境	
Global Pivotal Study 全球多中心	☹
Regional Study 区域性多中心	☹
China Alone Clinical Study中国独立临床	☹



To be forced to traditional CTA filing as Cate III drug
传统的三类药提交，导致4-6年的药物滞后现象？

Clinical Trial Execution
临床试验的开展

Clinical Trial Execution
临床试验的开展

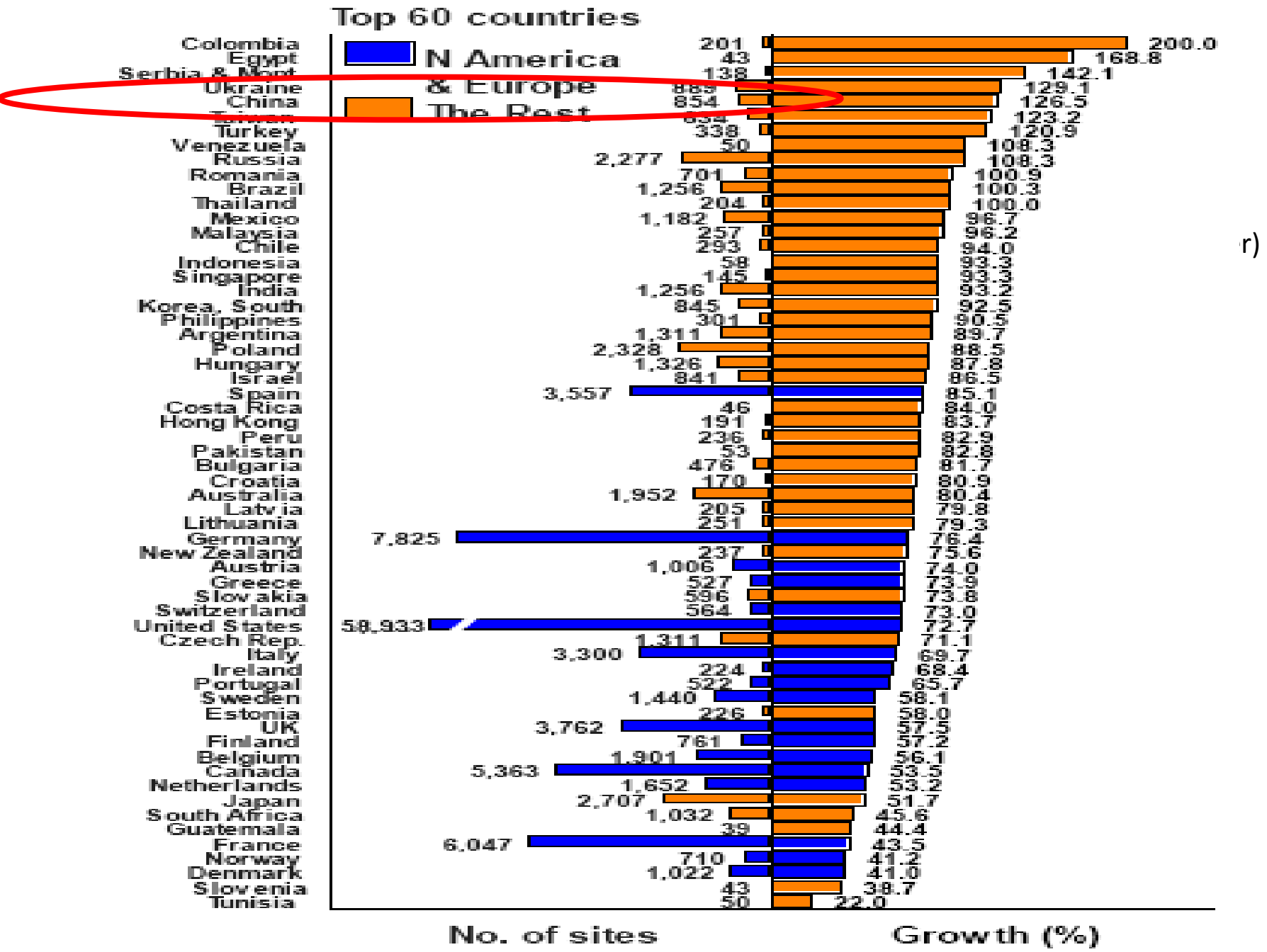
- IEC approval cannot approve CT in parallel which delay CT initiation

  伦理委员会尚不能平行批准试验，从而延后试验开展
- Limited certified sites to be bottleneck

  有限的基地数量成为瓶颈
- Bio sample (with genetic data) exportation is big issue

  含遗传信息的生物样品出口仍是大问题
- Huge custom tax charged for clinical sample is unreasonable

  海关对于临床样品的巨额关税 缺乏合理性


Top 60 countries
N America & Europe
The Rest
Colombia 201 200.0
Egypt 43 168.8
Serbia & Mont 138 142.1
Ukraine 889 129.1
China 854 126.5
Taiwan 634 123.2
Turkey 338 120.9
Venezuela 50 108.3
Russia 2,277 108.3
Romania 701 100.9
Brazil 1,256 100.3
Thailand 204 100.0
Mexico 1,182 96.7
Malaysia 257 96.2
Chile 293 94.0
Indonesia 58 93.3
Singapore 145 93.3
India 1,256 93.2
Korea, South 845 92.5
Philippines 301 90.5
Argentina 1,311 89.7
Poland 2,328 88.5
Hungary 1,326 87.8
Israel 841 86.5
Spain 3,557 85.1
Costa Rica 46 84.0
Hong Kong 191 83.7
Peru 236 82.9
Pakistan 53 82.8
Bulgaria 476 81.7
Croatia 170 80.9
Australia 1,952 80.4
Latvia 205 79.8
Lithuania 251 79.3
Germany 7,825 76.4
New Zealand 237 75.6
Austria 1,006 74.0
Greece 527 73.9
Slovakia 596 73.8
Switzerland 564 73.0
United States 58,933 72.7
Czech Rep. 1,311 71.1
Italy 3,300 69.7
Ireland 224 68.4
Portugal 522 65.7
Sweden 1,440 58.1
Estonia 226 58.0
UK 3,762 57.5
Finland 761 57.2
Belgium 1,901 56.1
Canada 5,363 53.5
Netherlands 1,652 53.2
Japan 2,707 51.7
South Africa 1,032 45.6
Guatemala 39 44.4
France 6,047 43.5
Norway 710 41.2
Denmark 1,022 41.0
Slovenia 43 38.7
Tunisia 50 22.0
No. of sites
Growth (%)

r)

Positive Move
可能的新气象

- First In Human 首次上人试验的突破
  - FIH as priority project of CDE in 2012
    FIH 作为CDE2012 年的重点项目之一
  - First open to oncology/TB/HIV TA
    可能首先对于肿瘤/结核病/艾滋病等领域开放
  - Need whole system cooperation
    需要全体系的配合

Thanks

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