Understanding the Research and Development Process

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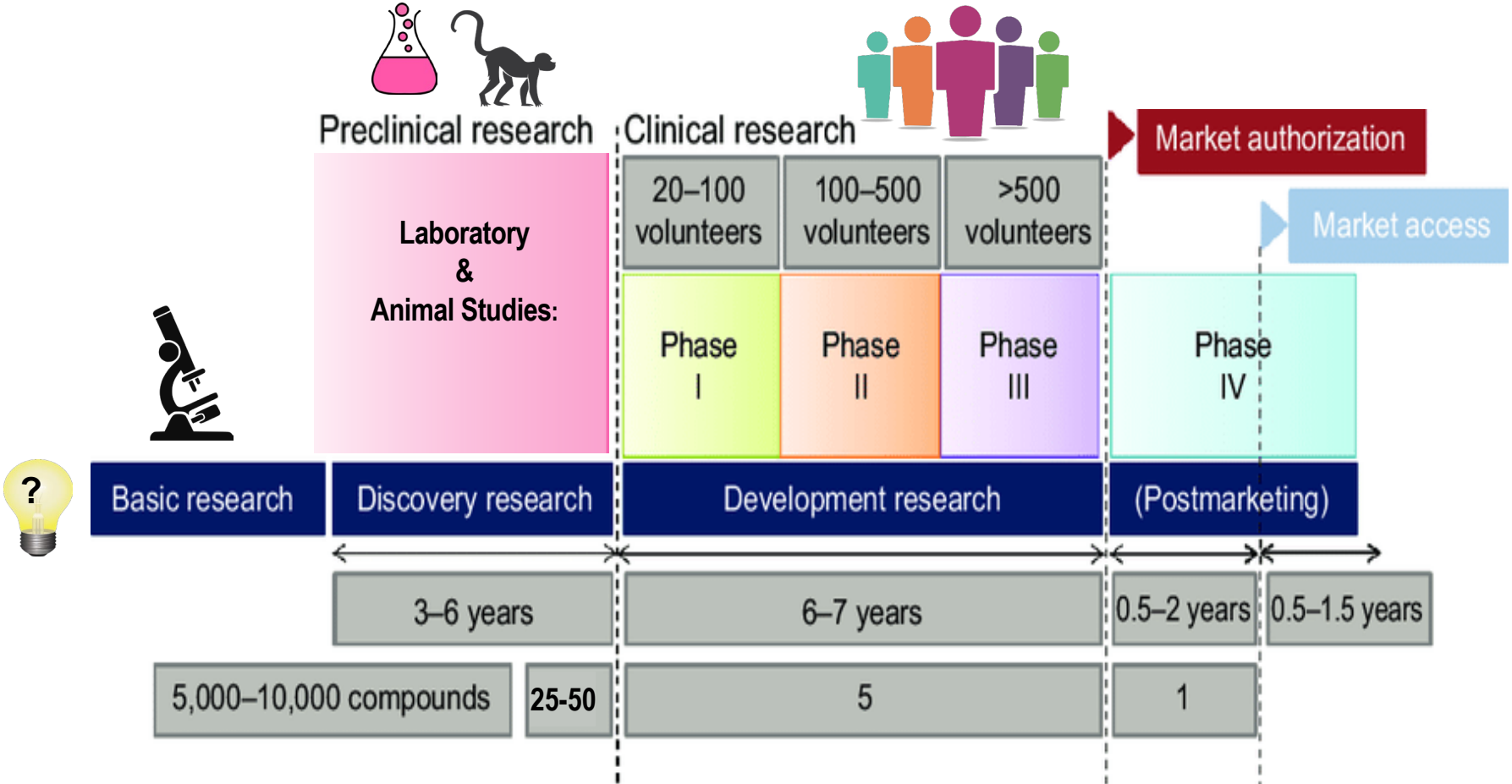
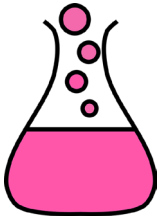
A long and complex process

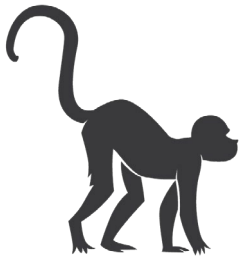
- It's a long and complex process that can take 10-15 years for a candidate to make its way from laboratory to regulatory approval
- Failure is more common than success, however
  - Of 10,000 ideas at the discovery stage, only 1 will be approved for licensure
  - Only 1 of 10 candidates that makes it to clinical trials will succeed
  - Failure may happen at any step along the way
  - May be due to poor efficacy, safety concerns, drug mechanisms or lack of strategic planning that would make for its practical delivery

The Research and Development Process



What happens during pre-clinical research?





- Preclinical research involves laboratory and animal studies that look at the safety (toxicology), mechanism of action, dosage and formulation
- Potential compounds are examined in cell culture, in computer models, and with other tools; and researchers look to optimize the particular formulation or product for the next step – animal studies.
- Tests in animals are conducted to determine whether the product works the way researchers think it should, and if it is safe.
- If the results of these preclinical studies suggest the product is safe and effective, the developer will need to file an Investigational New Drug (IND) application seeking regulatory approval to begin trials in humans

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Stages of HIV Clinical Trials

PHASE I

12 to 18 months

Small group **(20-100 people)** of healthy, HIV negative participants to test **safety** and **acceptability** of the product and **drug distribution and absorption** (how and where the drug is taken up in the body).

PHASE II

Up to 2 years

Hundreds (100-500) of HIV negative participants to test **safety**, seek **best dose** for **potential efficacy**

PHASE III

3 to 4 years

Often more than 1,000 participants at risk to evaluate **safety** and **efficacy**. Two Phase III trials are needed to **support approval of the product.**

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How many trials are conducted?

- More than one Phase 1 and Phase 2 study may be conducted of a product before advancing to Phase 3.
- Two Phase 3 studies are usually required by drug regulatory authorities to support approval of a product.

- For the dapivirine ring, IPM's application to the European Medicines Agency included data from:
  - 183 preclinical studies
  - 11 Phase 1 and Phase 2 safety and pharmacokinetics trials
  - 2 Phase 3 trials
  - (Results from 33 additional studies were submitted as supplemental information)

Research must be conducted according to rigorous standards

- **Good Laboratory Practice (GLP)** regulates the processes and conditions under which clinical and non-clinical research is conducted. GLP also governs how these research facilities should be maintained.
- **Good Clinical Practice (GCP)** guidelines are dictated by the International Conference on Harmonization (ICH) and are concerned with the ethical and scientific quality of clinical trials.
- **Good Manufacturing Practice (GMP)** regulates the design, monitoring, and control of manufacturing processes and facilities to ensure the quality and purity of products.

Good Participatory Practice (GPP) is also very important!

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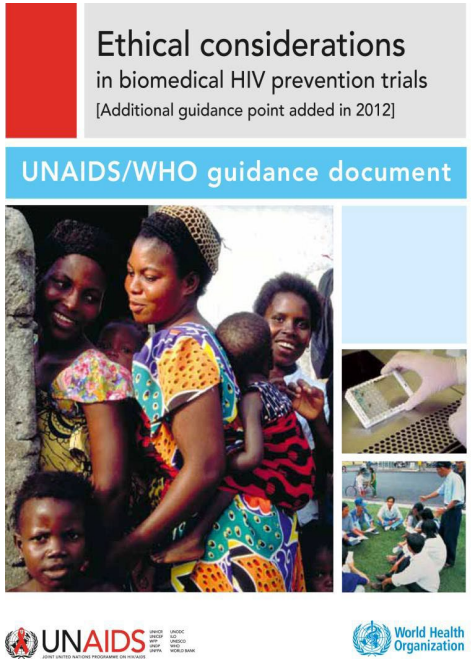
Do no harm: Ensuring participant safety and ethical conduct of trials



Different entities provide oversight of clinical trial conduct:

- National regulatory authorities
- Institutional Review Boards/Ethics Committees
- Data Safety and Monitoring Boards (for Phase III trials)
- Community Advisory Boards

Ensuring the welfare of research participants is the primary goal

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In summary

- Research and development is a long and complicated process.
- Success is not a given.
- Rigorous standards ensure participant safety and the integrity of the research process and the resulting data.

Acknowledgements

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