Patient-Focused Drug Development

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FDA B-R Framework Identifies 5 Key Considerations

- Through case study analysis, several key considerations were identified that cut across different regulatory decisions:
  - Severity of Condition
  - Unmet Medical Need
  - Benefit
  - Risk
  - Risk Management
- **Severity of Condition** and **Unmet Medical Need** provide regulators with the clinical context for weighing benefits and risks and the associated uncertainties
- **Benefit** and **Risk** incorporate expert judgments based on evaluation of the efficacy and safety data
- **Risk Management** incorporates expert judgments on the expected impact of efforts to reduce and further characterize risks

Patient Perspective: Patient-Focused Drug Development

- Assessment of a drug's benefits and risks involves analysis of severity of condition and current state of the treatment armamentarium
- Patients who live with a disease have a direct stake in drug review process and are in a unique position to contribute to drug development
- Review process could benefit from systematic approach to obtaining patient perspective on disease severity or unmet medical need

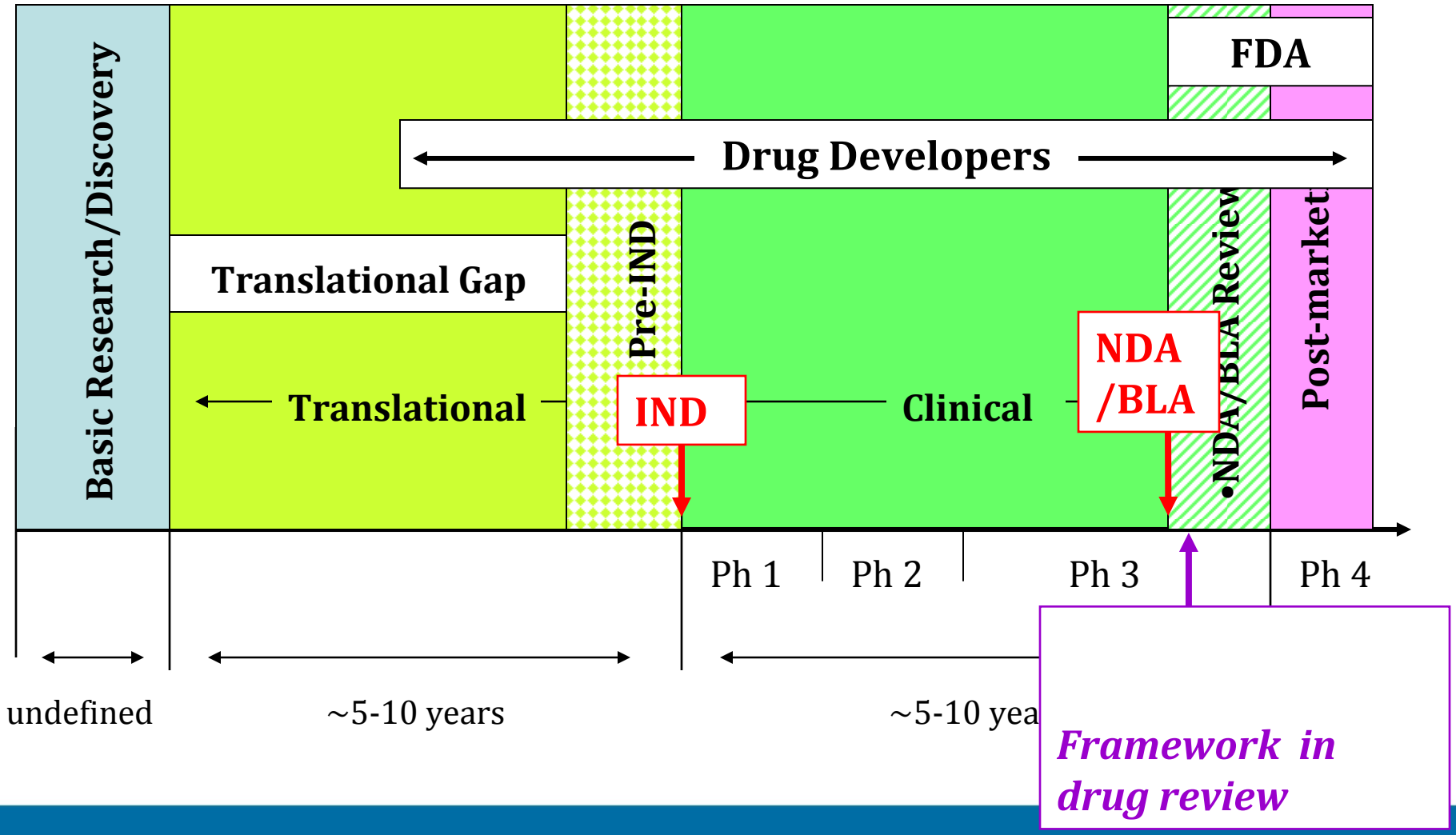
PDUFA V
Patient-Focused Drug Development

FDA has proposed a systematic effort in PDUFA V:

- PDUFA V provides resources to support additional program staff to expand activities dedicated to providing review divisions with patient input
- FDA will convene meetings with participation from review divisions, the relevant patient advocacy community, and other interested parties
- FDA will hold four public workshops per year—a total of 20 meetings over 5 years
  - Each meeting will focus on a different disease area, reviewing the armamentarium for that indication, and identifying areas of unmet need

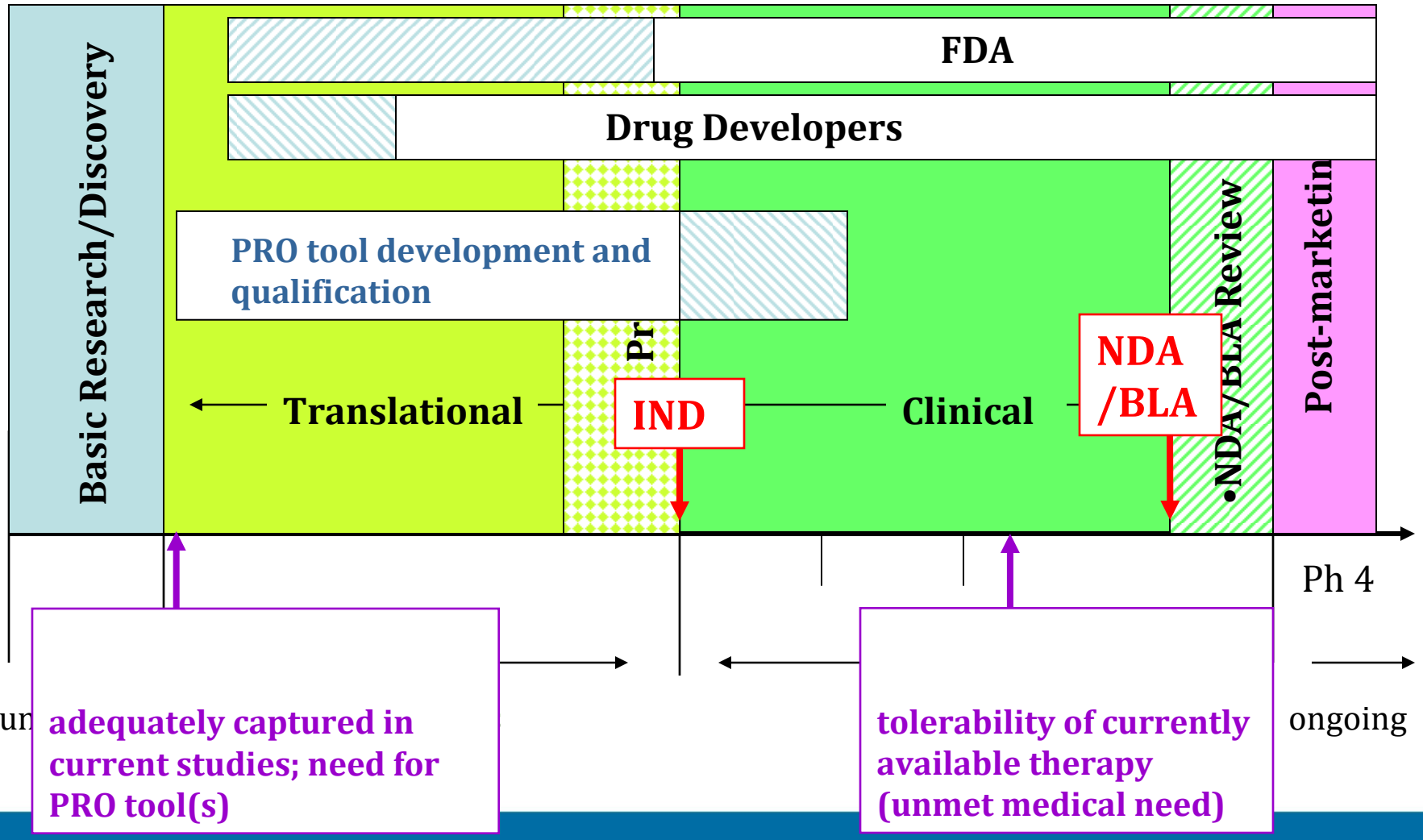
Enabling more patient-focused *drug development*

Drug Development and Review



Patient-focused development

For a specified disease area



Benefit-Risk Assessment Framework: Analysis of Condition

Assessing Evidence and Uncertainties– for a given drug for a given indication-- questions for FDA to consider include

- *What is the treated (or prevented) condition?*
- *What are its clinical manifestations (i.e., symptoms that are either reported or observed)?*
- *What is known about the natural history and progression of the condition, including in specific subpopulations?*
- *How severe is the condition for those who have it?*
  - *How does severity vary across the sub-populations we have defined? (Note specific subpopulations and nature of differences.)*
- *What is the basis for our assessment of the condition and its severity? (Note any relevant literature, clinical experience, expert opinion, etc.)*
- *What are the major uncertainties in the available information? What are their implications?*

Benefit-Risk Assessment Framework: Unmet Medical Need

Assessing Evidence and Uncertainties –for a given drug for a given indication-- questions for FDA to consider include

- *What other pharmacological therapies are approved for this condition?*
- *How effective are these alternative therapies?*
  - *How does their effectiveness vary by sub-population?*
- *How well tolerated are these alternative therapies?*
  - *How does tolerance vary by sub-population?*
- *What off-label pharmacological therapies might be considered?*
  - *How effective and how well tolerated are they reported or believed to be?*
- *What non-pharmacological therapies might be considered?*
  - *How effective and how well tolerated are they reported or believed to be?*
- *What kinds of evidence are available about the use of alternative treatments for this condition?*
- *What is the strength of evidence in each case?*
- *What are the major uncertainties in the evidence? What are their implications?*

Patient-Reported Outcome (PRO) Measure

- Any report of the status of a patient's health condition coming directly from the patient, without interpretation by physicians or anyone, about how the patient functions or feels in relation to a health condition and its treatment

FDA Review of PRO Instruments

Does the instrument measure the concept it is supposed to measure?

- Well-specified and reliable
- Specific for target population
- Specific for target indication
- Adequate measurement properties
  - E.g., content validity

Qualitative research can be used to establish PRO content validity

- This might include:
  - Focus groups to generate a pool of patient outcome-related domains and their components
    - What symptoms and functions or activities impacted by disease that are most important to patients
  - Surveys including a larger and more diverse sample patients with a given condition
    - E.g., examine the importance and relevance of domains identified by literature review, expert opinion or among a smaller set of patients, to validate these items and perhaps explore other measurement characteristics

Example: People with Chronic Pain

- Focus groups conducted with patients who experience chronic pain identified 19 aspects of their lives (outcome domains) that are significantly impacted by the presence of their symptoms and for which improvements were important criteria that they use in evaluating the effectiveness of any treatment*

Falling asleep at night	Participating in recreational/social activities
Staying asleep at night	Physical activities (walking, climbing stairs, etc.)
Sex life	Hobbies
Taking care of family	Enjoyment of life
Relations with family	Emotional well-being (feeling sad, etc.)
Relations with friends	Fatigue, feeling tired
Employment	Weakness
Household activities, running errands	Difficulty concentrating
Planning activities	Difficulty remembering things
Participatin in family events/activities	

*"Identifying important outcome domains for chronic pain clinical trials: An IMMPACT survey of people with pain", D.C. Turk et al., *Pain*, 137 (2008) 276-285

Next Steps
Patient-Focused Drug Development

- Summer 2012:
  - Develop preliminary list of 20 disease areas for public comment to inform planning for the set of 20 PDUFA V meetings
  - Develop basic roadmap that could be used by patient groups interested in pursuing need for and development of PRO measures in a specific disease area
    - Identify important but currently unaddressed aspects of their disease experience to potentially be considered in evaluating new therapies
- September 2012
  - Publish FR notice with preliminary list of 20 disease areas for public comment
- October 2012
  - Plan to hold public meeting to:
    - Discuss the proposed list of disease areas for the PDUFA meetings and get public input
    - Discuss strategies for getting broader public input and basic roadmap for identification of important patient outcomes and strategies for collaborative development PRO measures

The Patient-Focused Drug Development initiative

Will add to the existing FDA programs designed to integrate patients' perspectives

FDA's Patient Advocacy Programs

Office of Special Health Issues

- Patient Representation Program

FDA Patient Representative Program

Role of the FDA Patient Representative:

- Provide FDA with the unique perspective of patients and family members directly affected by serious or life-threatening disease.
- Serve in several ways, including:
  - On Advisory Committees, where they offer the patient perspective, ask questions, and give comments to assist the committee in making recommendations.
  - As consultants for review divisions – the clinicians and scientists who review data submitted to determine whether the product's benefits outweigh the potential risks
  - As presenters at FDA meetings and workshops on disease-specific or regulatory and health policy issues

FDA Patient Representative Program (cont.)

The Program's Activities:

- Recruitment of New Patient Representatives
- Selection of Patient Representatives for:
  - Advisory Committees
  - Consultation with Review Division
- Conducts Training For Patient Representatives
  - Individual FDA 101 Training
  - Monthly Webinars
  - Annual Workshop for Newly Recruited Patient Representatives
- More information: http://www.fda.gov/forconsumers/byaudience/forpatientadvocates/patientinvolvement/ucm123858.htm

What Does the FDA Look For?

Someone who brings a personal viewpoint to the process and communicates a collective patient perspective

- A patient perspective is created when a person goes through personal experience with the disease
- A collective patient perspective is created when the person has knowledge of others' disease experiences and conveys this collective patient perspective

APPENDIX
More Information about FDA's Patient Representative Program

Patient Representative Program

- Patient Representative provide Advisory Committee and FDA insight on issues, problems, and/or questions pertinent to the viewpoint of patients and family members living with a specific serious or life-threatening disease.
  - Personal experience with/knowledgeable about the specific illness
  - Ability to articulate the perspective of patients
  - Experience as a patient advocate
  - Formal affiliation with a patient advocacy organization
  - The ability to identify issues through communication with patient constituencies
- Serve on AC when a product or therapy related to specific illness is under review, as either voting or non-voting member
  - Voting: must be appointed as special government employees (SGEs); requires disclosure of personal financial information to the FDA in order to determine whether their financial interests pose a possible conflict of interest on an advisory committee
  - Non-voting: may only vote on procedural matters concerning the conduct of the meeting
  - In both cases: expected to provide the patient perspective, ask questions, and offer comments to assist the committee in making recommendations

Drug Development Patient Consultant Program

- Incorporates the perspective of patient advocates into the drug development process; allows opportunity to participate in the FDA drug review regulatory process.
- Selected to participate in meetings by matching a specific illness and proposed indication for the new therapeutic drug being developed.
- Participate in meetings (via telephone) between the FDA and drug companies.
  - Newly selected patient consultant receive training and participate in monthly telephone lecture series in preparation for these meetings.
  - To provide consultation to both FDA and the drug company, it is important that the patient consultant have background information on the drug under review.
  - ~3 weeks before each meeting, the patient consultant is mailed the meeting package containing the meeting issues and questions. The patient consultant reviews the meeting package in preparation for the meeting.