

# Roadmap Target #2: Bioassay Review and Redesign

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## Roadmap Target #2: Bioassay Review and Redesign **EVALUATION OF BASIC STUDY DESIGN**

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1. reevaluate strains and species used in bioassays, including transgenics (high)
  - conduct or collaborate on a workshop to develop recommendations (2006)
  - present NTP assessment to BSC (2007)
2. reevaluate timing and duration of exposure (high)
  - conduct or collaborate on a workshop to develop recommendations (2006)
  - present NTP assessment to BSC (2007)
3. evaluate the need for satellite groups for mechanistic/dosimetry studies (high)
  - conduct or collaborate on a workshop to develop recommendations (2006)
  - present NTP assessment to BSC (2007)

## Roadmap Target #2: Bioassay Review and Redesign **EVALUATION OF BASIC STUDY DESIGN**

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4. expand use of bioassays to address principle-based questions (e.g., mixtures, age, sensitive subpopulations, c\*t)(high)
  - actively solicit nominations for critical principles from interested stake holders (early 2005)
5. evaluate basic designs to incorporate consideration of the three R's (high)
  - ongoing

# Roadmap Target #2: Bioassay Review and Redesign **DOSE/DOSIMETRY**

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1. where possible, include tissue dosimetry and pharmacokinetics in bioassays for the purpose of linking to human biomonitoring (high)
  - conduct or collaborate on a workshop to identify appropriate dose metrics (2005-2006)
  - develop criteria for which compounds to target for dosimetry, present to BSC for review (2006)
  - implementation (2007)
2. reevaluate dose selection to improve utility in human health risk assessment, including reevaluating the definition of MTD (high)
  - monitor ongoing ILSI and other dose selection activities (2004)
  - present implications of that review on bioassay design to the BSC (late 2005)

## Roadmap Target #2: Bioassay Review and Redesign **EVALUATION OF ENDPOINTS**

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1. add more descriptive pathology to subchronic bioassays (high)
  - develop new protocols (2005)
  - conduct training (2006)
  - implement (2007)
2. develop a strategy to identify and incorporate mechanistic endpoints into bioassays (high)
  - develop proposal for strategy (2006 or when mechanistic targets are identified)
  - collaborate on a workshop to review proposal (2006)
  - refine proposal for BSC review (2007)
  - implementation (2007)
3. evaluate endpoint assessment to incorporate consideration of the three R's (high)
  - ongoing

## Roadmap Target #2: Bioassay Review and Redesign **EVALUATION OF ENDPOINTS**

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4. evaluate addition of functional endpoints of human clinical relevance (medium)
  - establish a collaborative research program(s) to identify endpoints that can be evaluated trans-species (2004)
  - develop a report identifying most likely candidates for inclusion for BSC review (2006)
5. refine existing clinical pathology endpoints, including biomarkers of exposure and effect (medium)
  - review current endpoints and develop recommendations on additional endpoints (late 2005)
  - present to BSC (early 2006)
6. expand non-invasive interim assessments (medium)
  - conduct or collaborate on a workshop, include consideration of 3 R's (2005-2006)
  - present to BSC (2006)
  - implementation (2007)

## Roadmap Target #2: Bioassay Review and Redesign **RETROSPECTIVE ANALYSIS**

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1. **conduct selective reevaluation of pathology of older 2-year bioassays (and corresponding subchronic studies) using current pathology standards (high)**
  - **by 2005 develop a strategy to determine sequence and scope of reevaluation (BSC review)**
  - **complete reevaluation by 2008**
2. **selective reevaluation of older bioassays focusing on additional endpoints (low)**
  - **as needed and if possible**

## Roadmap Target #2: Bioassay Review and Redesign **IMPROVING THE PROCESS**

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1. conduct review of composition and effectiveness of study design and evaluation teams (high)
  - begin (early 2005)
  - draft new guidelines on team composition (2005)
2. refine the process to ensure consideration of pre-chronic findings into the chronic bioassay design (high)
  - begin immediately
3. develop seamless and flexible process for data acquisition, storage and retrieval for integrated analysis (high)
  - continue ongoing activities
4. establish process to identify and nurture new assay technologies (medium)
  - continue to work with ICCVAM and DERT to identify creative solutions



## Roadmap Target #2: Bioassay Review and Redesign **IMPROVING THE PROCESS**

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5. streamline the pathology peer-review and quality assurance process (medium)
  - present proposed new process to BSC (2005)
6. digitize pathology images (medium)
  - present plan for prioritization to BSC (2005)
7. begin permanent archiving of all pathology samples to facilitate retrospective analyses (low)
  - begin immediately

# Roadmap Target #2: Bioassay Review and Redesign **EVALUATION OF BASIC STUDY DESIGN**

	strains/species	timing/duration	satellite groups	principle-based questions	three R's
2005				Solicit nominations stake holders	Ongoing
2006	Workshop	Workshop	Workshop		
2007	BSC review	BSC review	BSC review		

# Roadmap Target #2: Bioassay Review and Redesign **DOSE/DOSIMETRY**

	tissue dosimetry	dose selection
2005	Workshop	monitor ongoing ILSI and other dose selection activities
2006	BSC Review	BSC Review Workshop
2007	Implement	

# Roadmap Target #2: Bioassay Review and Redesign **EVALUATION OF ENDPOINTS**

	descriptive pathology	incorporate mechanistic endpoints	three R's	functional endpoints	clinical pathology endpoints	non-invasive interim assessments
2005	Develop new protocols		Ongoing	Establish collaborative research program(s)		
					NTP Review	Workshop
2006	Conduct training	Develop proposal		BSC Review	BSC Review	BSC Review
		Workshop				
2007	Implement					Implement
		BSC review				
2008		implement				

# Roadmap Target #2: Bioassay Review and Redesign **RETROSPECTIVE ANALYSIS**

	reevaluate pathology of older 2-year bioassays	reevaluate of older bioassays focusing on additional endpoints
2005	BSC Review	As needed and if possible
2006		
2007		
2008	Complete evaluation	

# Roadmap Target #2: Bioassay Review and Redesign **IMPROVING THE PROCESS**

	study design teams	pre-chronic findings	databases	new assay technologies	pathology peer-review	digitize pathology images	archiving
2005	Complete review	Begin	Continue	Continue to work with ICCVAM and DERT to identify creative solutions			Begin
2006	Draft new guidelines				BSC Review	BSC Review	