

# Viability Primary Screen IMPC\_VIA\_001

## Purpose

To assess the postnatal viability, sub-viability, and lethality of homozygous mice during cohort production.

## Experimental Design

- Monitor genotypes of Het X Het breeding units; score genotypes of at least 28 live pups, unless four or more hom pups are produced before this threshold is reached. (if other breeding strategies are used specify in the metadata and follow this convention HomXHet FemaleXMale)
- Definition of female age: "Female age earliest start/Female age oldest end" age of the youngest and oldest female mouse respectively when cohort breeding starts
- Age to be genotyped: P1-P28
- Record sex ratios of pups
- Collect and report all litters and genotype data: flag strains that produce no homozygote pups
- Identify and score lethals (defined as no homozygotes at genotype)
- Identify subviables (defined as <50% of expected homozygotes)
- If homozygous lethal: perform the embryonic lethal pipeline (if available)

## Procedure

1. Monitor pup number, genotypes and sex ratios of Het X Het intercrosses set to generate cohorts for phenotyping. Score at least 28 live pups when genotyped, unless four or more hom pups are produced before this threshold is reached.
2. Identify strains that produce no homozygous/hemizygous male or female pups.
  - a. Strains that produce NO homozygous pups will be considered LETHAL (complete preweaning lethality [MP: 0011100]).
  - b. X-linked strains that produce NO hemizygous male pups and NO female homozygous pups will be considered LETHAL (complete preweaning lethality [MP: 0011100]).
  - c. These will undergo embryonic lethal pipeline (if available)
3. Identify strains that produce less than normal numbers of homozygous/hemizygous male or female pups.
  - a. Strains that produce <50% expected ( $\#totalpups * 0.125$  (3 for 28) (4 for 29-36) (5 for 37-52) (See stats table in Notes)) homozygous pups will be considered SUBVIABLE (partial preweaning lethality [MP: 0011110]).
  - b. X-linked strains that produce <50% expected ( $\#totalpups * 0.125$  (3 for 28) (4 for 29-36) (5 for 37-52) (See stats table in Notes)) hemizygous male pups and female homozygous pups will be considered SUBVIABLE (partial preweaning lethality [MP: 0011110]).
  - c. Some centers will proceed with secondary screening.
4. For lethal and subviable strains, heterozygous progeny will be sent for adult phenotyping.

# Notes

All genotypes should be collected using validated assays.  
Line level calls will be rejected until 28 mice have been genotyped, unless four or more hom pups are produced before this threshold is reached, in which case a viable call is valid.

Sub-viable significance table:

Number genotyped	Pups observed	Formula (Excel)	P-value
28	3	=BINOMDIST(3,28,0.25,1)	0.055135567
29	4	=BINOMDIST(4,29,0.25,1)	0.115324345
30	4	=BINOMDIST(4,30,0.25,1)	0.0978696
31	4	=BINOMDIST(4,31,0.25,1)	0.082764531
32	4	=BINOMDIST(4,32,0.25,1)	0.069757389
33	4	=BINOMDIST(4,33,0.25,1)	0.05860841
34	4	=BINOMDIST(4,34,0.25,1)	0.049093333
35	4	=BINOMDIST(4,35,0.25,1)	0.041005517
36	4	=BINOMDIST(4,36,0.25,1)	0.034156964
37	5	=BINOMDIST(5,37,0.25,1)	0.071139152
38	5	=BINOMDIST(5,38,0.25,1)	0.060448988
39	5	=BINOMDIST(5,39,0.25,1)	0.051216574
40	5	=BINOMDIST(5,40,0.25,1)	0.043273983
41	5	=BINOMDIST(5,41,0.25,1)	0.036466047
42	5	=BINOMDIST(5,42,0.25,1)	0.030650935
43	5	=BINOMDIST(5,43,0.25,1)	0.025700232
44	5	=BINOMDIST(5,44,0.25,1)	0.021498648
45	5	=BINOMDIST(5,45,0.25,1)	0.017943462
46	5	=BINOMDIST(5,46,0.25,1)	0.014943774
47	5	=BINOMDIST(5,47,0.25,1)	0.012419646
48	5	=BINOMDIST(5,48,0.25,1)	0.010301181
49	5	=BINOMDIST(5,49,0.25,1)	0.008527583
50	5	=BINOMDIST(5,50,0.25,1)	0.007046225
51	5	=BINOMDIST(5,51,0.25,1)	0.005811761
52	5	=BINOMDIST(5,52,0.25,1)	0.004785276

# Parameters and Metadata

Total pups IMPC\_VIA\_003\_001 | v1.1

simpleParameter

Req. Analysis: false

Req. Upload: true

Is Annotated: false

Unit Measured: count

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**% male WT** IMPC\_VIA\_020\_001 | v1.1

simpleParameter

Req. Analysis: false

Req. Upload: false

Is Annotated: false

Unit Measured: %

Derivation:  $\text{div}(\text{'IMPC\_VIA\_007\_001'}, \text{'IMPC\_VIA\_010\_001'})$

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**% female heterozygous** IMPC\_VIA\_024\_001 | v1.1

simpleParameter

Req. Analysis: false

Req. Upload: false

Is Annotated: false

Unit Measured: %

Derivation:  $\text{div}(\text{'IMPC\_VIA\_012\_001'}, \text{'IMPC\_VIA\_014\_001'})$

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**P-value for outcome call** IMPC\_VIA\_032\_001 | v1.2

simpleParameter

Req. Analysis: false

Req. Upload: false

Is Annotated: false

Derivation: unimplemented("")

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## Total pups homozygous IMPC\_VIA\_006\_001 | v1.0

simpleParameter

Req. Analysis: false

Req. Upload: true

Is Annotated: false

Unit Measured: count

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## Free Comment IMPC\_VIA\_016\_001 | v1.0

simpleParameter

Req. Analysis: false

Req. Upload: false

Is Annotated: false

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## Total male pups IMPC\_VIA\_010\_001 | v1.0

simpleParameter

Req. Analysis: false

Req. Upload: true

Is Annotated: false

Unit Measured: count

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## Total female WT IMPC\_VIA\_011\_001 | v1.0

simpleParameter

Req. Analysis: false

Req. Upload: true

Is Annotated: false

Unit Measured: count

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## Viability Outcome IMPC\_VIA\_001\_001 | v1.1

simpleParameter

Req. Analysis: false

Req. Upload: true

Is Annotated: true

Options: Homozygous - Viable, Homozygous - Lethal, Homozygous - Subviable, Hemizygous - Lethal, Hemizygous - Viable,

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## Total pups heterozygous IMPC\_VIA\_005\_001 | v1.0

simpleParameter

Req. Analysis: false

Req. Upload: true

Is Annotated: false

Unit Measured: count

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## % pups WT IMPC\_VIA\_015\_001 | v1.3

simpleParameter

Req. Analysis: false

Req. Upload: false

Is Annotated: false

Unit Measured: %

Derivation: div('IMPC\_VIA\_004\_001', 'IMPC\_VIA\_003\_001')

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**Total pups WT** IMPC\_VIA\_004\_001 | v1.1

simpleParameter

Req. Analysis: false

Req. Upload: true

Is Annotated: false

Unit Measured: count

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**% pups heterozygous** IMPC\_VIA\_018\_001 | v1.2

simpleParameter

Req. Analysis: false

Req. Upload: false

Is Annotated: false

Unit Measured: %

Derivation: div('IMPC\_VIA\_005\_001', 'IMPC\_VIA\_003\_001')

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**Time of dark cycle end** IMPC\_VIA\_029\_001 | v1.0

procedureMetadata

Req. Analysis: false

Req. Upload: true

Is Annotated: false

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## Total female heterozygous IMPC\_VIA\_012\_001 | v1.0

simpleParameter

Req. Analysis: false

Req. Upload: true

Is Annotated: false

Unit Measured: count

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## Additional Outcome IMPC\_VIA\_002\_001 | v1.1

simpleParameter

Req. Analysis: false

Req. Upload: false

Is Annotated: true

Options: Homozygous - Reduced Life Span, Homozygous - Sick Mouse,

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## Total female homozygous IMPC\_VIA\_013\_001 | v1.0

simpleParameter

Req. Analysis: false

Req. Upload: true

Is Annotated: false

Unit Measured: count

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## Female age oldest end IMPC\_VIA\_027\_001 | v1.1

procedureMetadata

Req. Analysis: false

Req. Upload: false

Is Annotated: false

Unit Measured: Weeks

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## Total female pups IMPC\_VIA\_014\_001 | v1.1

simpleParameter

Req. Analysis: false

Req. Upload: true

Is Annotated: false

Unit Measured: count

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## % female homozygous IMPC\_VIA\_025\_001 | v1.1

simpleParameter

Req. Analysis: false

Req. Upload: false

Is Annotated: false

Unit Measured: %

Derivation:  $\text{div}(\text{'IMPC\_VIA\_013\_001'}, \text{'IMPC\_VIA\_014\_001'})$

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## Age of pups at genotype IMPC\_VIA\_030\_001 | v1.1

procedureMetadata



Req. Analysis: false

Req. Upload: true

Is Annotated: false

Unit Measured: Weeks

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## Total male homozygous IMPC\_VIA\_009\_001 | v1.1

simpleParameter

Req. Analysis: false

Req. Upload: true

Is Annotated: false

Unit Measured: count

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## Additional Subviable Outcome IMPC\_VIA\_033\_001 | v1.1

simpleParameter

Req. Analysis: false

Req. Upload: false

Is Annotated: false

Options: Hemizygous - Subviable, Heterozygous - Subviable,

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## Breeding Strategy IMPC\_VIA\_031\_001 | v1.0

procedureMetadata

Req. Analysis: false

Req. Upload: true

Is Annotated: false

**Options:** HetXHem, HetXWT, HetXHet, HomXHet, HetXHom,

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## Total male WT IMPC\_VIA\_007\_001 | v1.0

simpleParameter

**Req. Analysis:** false      **Req. Upload:** true      **Is Annotated:** false

**Unit Measured:** count

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## % female WT IMPC\_VIA\_023\_001 | v1.1

simpleParameter

**Req. Analysis:** false      **Req. Upload:** false      **Is Annotated:** false

**Unit Measured:** %

**Derivation:** div('IMPC\_VIA\_011\_001', 'IMPC\_VIA\_014\_001')

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## % male heterozygous IMPC\_VIA\_021\_001 | v1.1

simpleParameter

**Req. Analysis:** false      **Req. Upload:** false      **Is Annotated:** false

**Unit Measured:** %

**Derivation:** div('IMPC\_VIA\_008\_001', 'IMPC\_VIA\_010\_001')

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## Total male heterozygous IMPC\_VIA\_008\_001 | v1.0

simpleParameter

Req. Analysis: false

Req. Upload: true

Is Annotated: false

Unit Measured: count

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## Female age earliest start IMPC\_VIA\_026\_001 | v1.1

procedureMetadata

Req. Analysis: false

Req. Upload: false

Is Annotated: false

Unit Measured: Weeks

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## Average litter size IMPC\_VIA\_017\_001 | v1.0

simpleParameter

Req. Analysis: false

Req. Upload: false

Is Annotated: false

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## % pups homozygous IMPC\_VIA\_019\_001 | v1.1

simpleParameter

**Req. Analysis:** false

**Req. Upload:** false

**Is Annotated:** false

**Unit Measured:** %

**Derivation:** div('IMPC\_VIA\_006\_001', 'IMPC\_VIA\_003\_001')

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**% male homozygous** IMPC\_VIA\_022\_001 | v1.1

simpleParameter

**Req. Analysis:** false

**Req. Upload:** false

**Is Annotated:** false

**Unit Measured:** %

**Derivation:** div('IMPC\_VIA\_009\_001', 'IMPC\_VIA\_010\_001')

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**Time of dark cycle start** IMPC\_VIA\_028\_001 | v1.1

procedureMetadata

**Req. Analysis:** false

**Req. Upload:** true

**Is Annotated:** false

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