

## Appendix B

# Phase-Transition Criteria

### The Quiet Biology Protocol

*Conditions under which the constraint-based framework is abandoned and conventional oncologic management initiated*

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## Governing Principle

The Quiet Biology Protocol is a constraint-based management framework, not a permanent alternative to oncologic care. It operates on a single governing condition: that AR signaling still matters, PSA still tells the truth, curvature stays slow, and the host remains strong. When any of those conditions ceases to hold, the framework ends.

This document defines the six phase-transition criteria — the hard biological signals that trigger abandonment of the constraint approach and transition to conventional oncologic management. These criteria are not thresholds to be negotiated. They are pre-committed decision rules, established in advance precisely because the moment of biological phase change is not the moment for deliberation.

*Escalation is not failure. It is the framework working as designed — remaining accountable to the biology rather than to the protocol.*

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## 1. Loss of AR Leverage

This is the most important criterion. The entire Quiet Biology framework depends on androgen receptor signaling remaining a meaningful biological lever. If AR no longer steers tumor growth, the hormonal coherence strategy loses its axis and Bipolar Androgen Therapy loses its mechanism.

### HARD CRITERIA

- PSA becomes unresponsive to testosterone changes across repeated cycles
- PSA becomes unresponsive to washouts
- PSA becomes unresponsive to AR perturbations
- Repeated cycles show no PSA rise with androgen increase and no PSA fall with androgen normalisation

### INTERPRETATION

If AR no longer moves PSA, AR is no longer steering growth. This is not stable disease. This is AR indifference — a qualitatively different biological state in which the foundational assumption of the protocol no longer holds.

| ● **Framework ends. Transition to oncologic review.**

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## **2. PSA–Biology Decoupling (Signal Failure)**

The entire monitoring architecture of Quiet Biology depends on PSA curvature as a reliable readout of biological system state. When that readout becomes unreliable, adaptive control is no longer possible. A misleading signal is more dangerous than no signal.

### **HARD CRITERIA**

- PSA remains flat or declining while LDH rises
- PSA remains flat or declining while ALP rises
- PSA remains flat or declining while clinical or imaging burden increases
- PSA kinetics no longer correlate with any other biological marker

### **INTERPRETATION**

This is not good control. This is loss of observability. Adaptive management requires a signal that reflects reality. When PSA decouples from the biology it is meant to represent, the framework has lost its primary instrument and cannot safely continue.

| ● **Stop finesse. Switch frameworks. Oncologic review.**

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## **3. Systemic Acceleration Despite Local Constraint**

This is the ecology lost signal. It indicates that the disease is changing character rather than merely changing size — that field-level containment has been lost and more aggressive phenotypes may be emerging independently of PSA-detectable AR-driven growth.

### **HARD CRITERIA**

- Sustained rise in LDH across multiple measurements — not noise, not a single reading
- Sustained rise in ALP across multiple measurements — not noise, not a single reading
- Pattern is especially significant when PSA remains slow or modest

### **INTERPRETATION**

Sustained independent rise in systemic aggressiveness markers implies a shift toward more aggressive phenotypes, possible lineage drift, or loss of field-level containment. The disease is behaving differently, not just growing. Containment logic is no longer the dominant biological dynamic.

| ● **Containment logic no longer dominant. Escalation indicated.**

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#### **4. Shortening PSADT with Curvature Change**

Slow PSA rise is tolerated. Accelerating curvature is not. This criterion is subtle but critical — it distinguishes between a tumor that is biologically contained at a slow tempo and one that is actively learning to escape constraint. It is the last exit before forced escalation.

##### **HARD CRITERIA**

- PSADT shortens materially across the full measurement series — not cherry-picked windows
- Shortening persists across washouts and cycling, not only within active blocks
- Especially significant when it occurs despite an unchanged strategy
- Curvature bending — acceleration of the acceleration — is the definitive signal

##### **INTERPRETATION**

When PSADT shortens across the full series and persists through washouts, a successful adaptive phenotype has stabilised within the tumor population. Evolution is no longer being constrained by the protocol. The window for non-escalatory management is closing.

| ● **Last exit before forced escalation. Begin oncologic review.**

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#### **5. Host Cost Exceeds Tumor Constraint**

Field control fails if the field collapses. The Quiet Biology framework depends not only on constraining the tumor but on the host remaining biologically capable of supporting and sustaining that constraint. A weakened host creates evolutionary slack even when the protocol is nominally unchanged.

##### **HARD CRITERIA**

- Recovery capacity declines and does not resolve during washout
- Exercise response collapses — capacity, tolerance, or adaptation to training falls materially
- Systemic inflammation or fatigue rises out of proportion to tumor signals
- Persistent immune susceptibility that does not clear during the washout phase

##### **INTERPRETATION**

This criterion operates independently of tumor biology. Even a nominally stable tumor becomes more dangerous in a declining host system. When the biological environment that was constraining the tumor begins to degrade, the constraint logic no longer holds regardless

of PSA kinetics. This is a reason to simplify and seek clinical support, not to intensify the protocol.

| ● **Simplify, do not intensify. Clinical review of host status.**

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## 6. Imaging Confirmation of Biological Phase Shift

Biologically triggered imaging is deployed in response to signal convergence from the other criteria, not on a calendar schedule. When it is deployed and shows a definitive phase shift, the framework ends regardless of PSA. Imaging finding is definitive — it is spatial and structural confirmation of what the kinetic signals have been suggesting.

### HARD CRITERIA

- New lesion types not present on prior imaging
- Visceral disease — liver, lung, or other visceral organ involvement
- Discordant lesion behavior — some lesions responding while others progress
- Any pattern inconsistent with AR-driven, field-constrained disease

### INTERPRETATION

This is definitionally a phase change regardless of PSA kinetics. The disease has crossed a biological threshold that PSA alone was not capturing. The framework ends here.

| ● **Framework ends. Transition to oncologic management.**

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## The Clean Rule Set

The framework is abandoned when any one of the following is true:

| # | Signal                | Abandonment criterion  | Status |
|---|-----------------------|--|--------|
| 1 | AR leverage           | AR no longer moves PSA across repeated cycles and washouts                         | RED    |
| 2 | Signal fidelity       | PSA flat or falling while LDH, ALP, or imaging burden rises                        | AMBER  |
| 3 | Systemic acceleration | Sustained independent rise in LDH and/or ALP across multiple readings              | RED    |
| 4 | PSA curvature         | PSADT shortens materially across full series, persisting through washouts          | AMBER  |
| 5 | Host resilience       | Recovery fails, exercise response collapses, inflammation rises disproportionately | AMBER  |

| # | Signal  | Abandonment criterion  | Status |
|---|---------|--|--------|
| 6 | Imaging | New lesion types, visceral disease, or discordant lesion behavior confirmed on imaging | RED    |

The framework is not abandoned because:

- PSA rises slowly within expected natural-history tempo
- Absolute PSA crosses a round-number threshold
- Numbers look uncomfortable without biological context
- External pressure favours non-standard strategies
- Time has passed without a clinical event

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## One-Sentence Summary

*The approach is sustained as long as AR still matters, PSA still tells the truth, curvature stays slow, and the host remains strong — and it is abandoned the moment any of those stop being true.*

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## Relationship to Companion Documents

This document defines the decision logic for framework abandonment. It is designed to be read alongside:

**The Quiet Biology White Paper** — the theoretical and empirical foundation establishing why constraint-based management is biologically defensible, and what biological phase change means in evolutionary oncology terms.

**Appendix A: The Author's Protocol** — the operational maintenance framework: compounds, doses, timing, cycling structure, and monitoring panel from which the signals assessed in this document are derived.

The three documents constitute a complete clinical submission: theoretical foundation, operational protocol, and escalation decision logic. The phase-transition criteria in this document are the mechanism by which the constraint-based framework remains accountable to the biology — and the guarantee that it does not become an ideology.