ArrowBiome®

ACNE SCIENCE SERIES · CHAPTER 6

Why Killing Bacteria Is Not the Answer

The science behind the next generation of acne care — why the old tools are no longer enough.

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A NOTE BEFORE YOU READ

The instinct we have never questioned

For more than four decades, acne treatment has rested on a single reflex: find the bacterium, and kill it. This briefing asks whether that reflex still serves the skin — and arrives at an uncomfortable answer.

WHAT THIS CHAPTER COVERS

From eradication to ecology

How acne science has moved from "kill the bug" to "restore the balance" — and what that means for short-term tolerability, long-term resistance, the global stewardship agenda, regulatory positioning, and the inflammatory cost of killing.

WHO IT IS FOR

A senior, non-specialist audience

Written for cosmetic brand managers, personal-care R&D directors, retail buyers and investor-relations contacts who want the science clearly — without the jargon, and without marketing spin.

THE SHORT VERSION

Conventional antibacterials work, but each carries an ecological cost — resistance, barrier damage, dysbiosis, and an inflammatory burst when cells are ruptured. The most defensible direction for the next generation of acne care is to **restore balance and physically remove persistence**, not wage indiscriminate chemical warfare on the skin.

A public educational piece from the ArrowBiome Knowledge Hub. Grounded in peer-reviewed evidence, 2015–2026. No product or brand claims.

INTRODUCTION

A Treatment Paradox

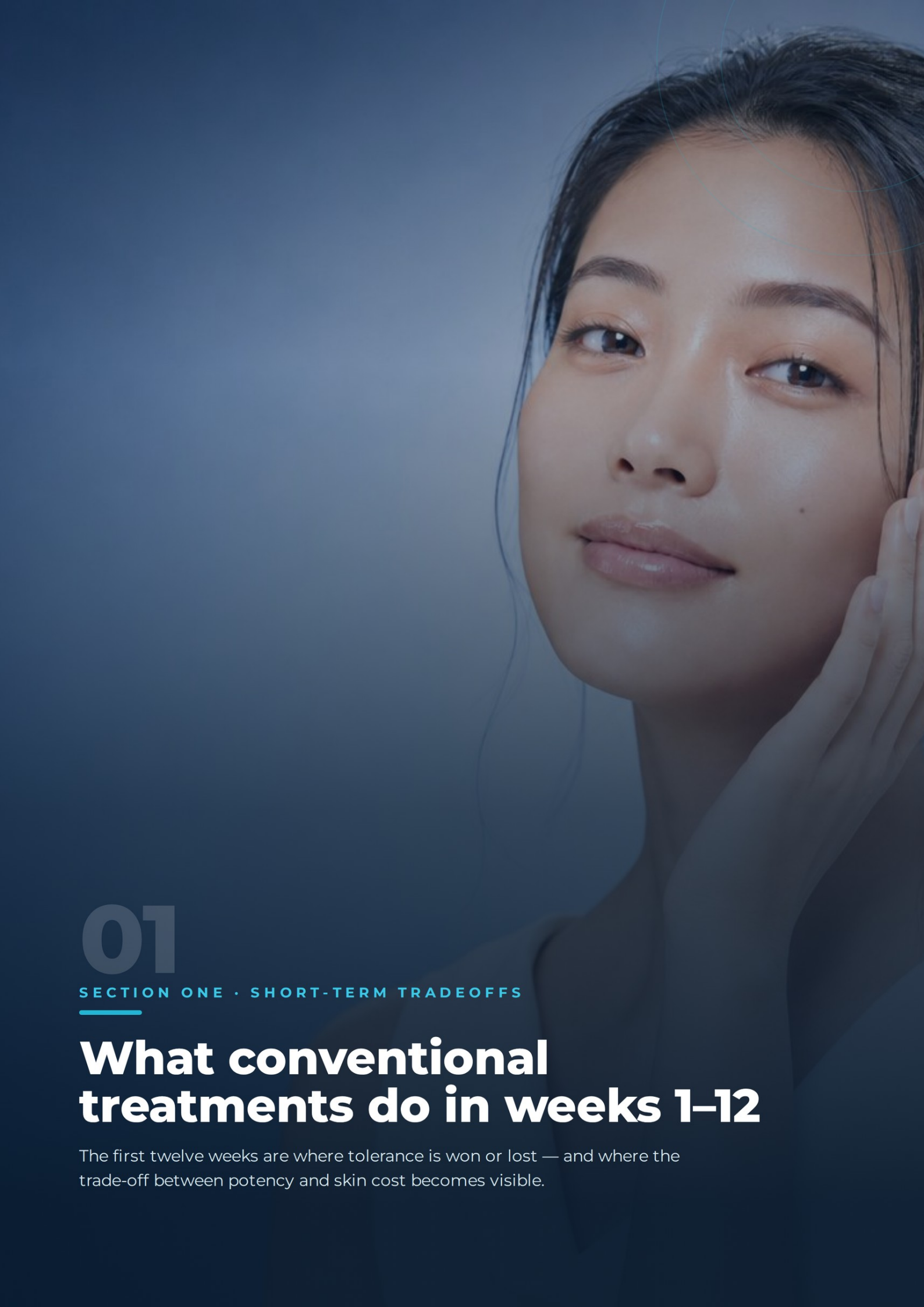
There is a quiet irony at the heart of modern acne care. The treatments designed to clear the skin can, over time, degrade the very ecosystem that keeps it healthy. Antibiotics select for resistant strains and thin out protective commensals; benzoyl peroxide raises water loss and strips the barrier it is applied to protect; and almost every conventional active leaves the biofilm-encased bacteria that drive relapse untouched. The harder a product works to eradicate, the more collateral damage it tends to inflict — and the more reliably acne returns once treatment stops.

THREE NUMBERS THAT FRAME THE CASE

1.27M
DEATHS ATTRIBUTABLE TO AMR, 2019

~64%
PEAK C. ACNES RESISTANCE RECORDED

~1.8×
TEWL RISE UNDER BENZOYL PEROXIDE



01

SECTION ONE · SHORT-TERM TRADEOFFS

What conventional treatments do in weeks 1–12

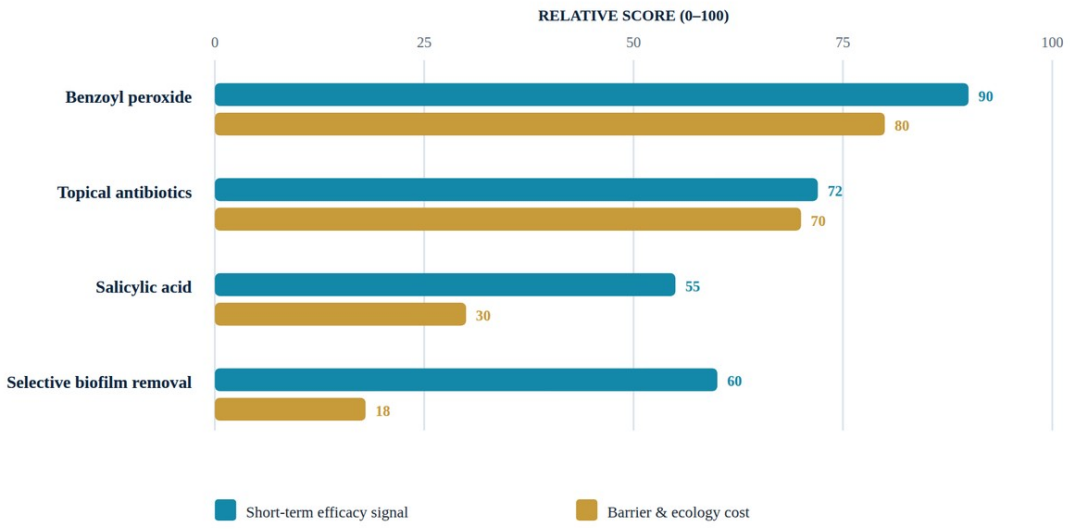
The first twelve weeks are where tolerance is won or lost — and where the trade-off between potency and skin cost becomes visible.

SHORT-TERM TRADEOFFS

Potency has a price

Benzoyl peroxide (BPO) carries the clearest short-term efficacy signal of any first-line topical — and the clearest irritancy burden. In a 12-week trial of 609 patients, drug-attributable skin exfoliation affected 19–24% of users, and a 10% formulation raises transepidermal water loss (TEWL) roughly 1.8-fold. **Topical antibiotics** feel gentle in week one but accrue an invisible cost as resistance and dysbiosis. **Salicylic acid** is better tolerated and microbiome-sparing, but its evidence base is thinner. Early **selective, non-lytic** approaches invert the usual trade-off — dismantling biofilm while sparing the barrier.

EFFICACY SIGNAL VS. BARRIER & ECOLOGY COST



REMEMBER THIS

The agent with the strongest short-term clearance, benzoyl peroxide, also carries the heaviest barrier and microbiome cost. **High efficacy and low collateral damage have, until now, pulled in opposite directions.**

Sources: AAD acne guidelines (Reynolds et al. 2024); Kawashima et al. 2017; Thiboutot & Del Rosso 2013; Wongtada et al. 2023; Crainic et al. 2025.

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SECTION TWO · THE LONG GAME

Resistance, rebound, and recovery

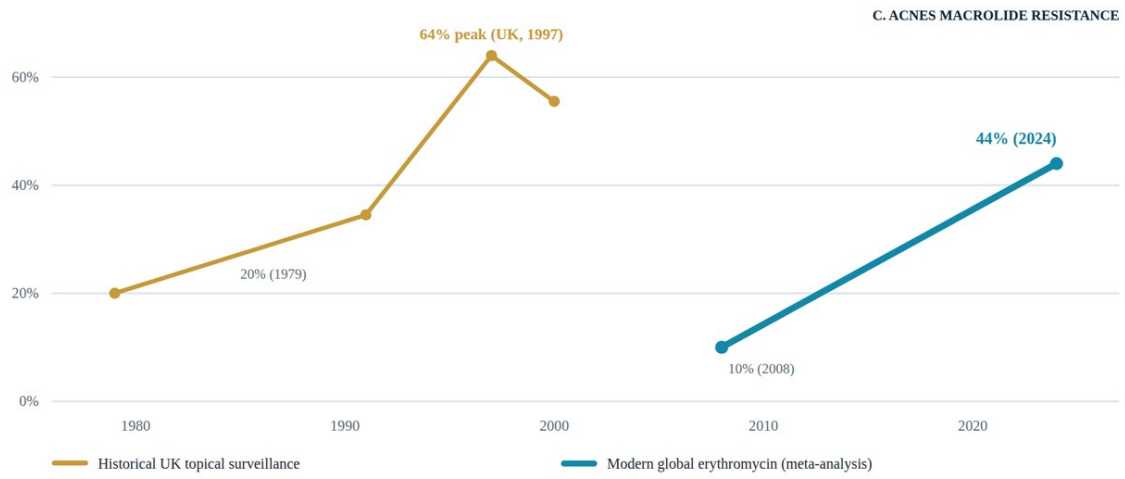
Over months and years, three liabilities compound: antibiotics select for resistance, the microbiome does not fully recover, and the biofilm reservoir seeds relapse.

THE LONG GAME

A five-decade trajectory

Resistance is the strongest long-term differentiator between treatment classes. In *Cutibacterium acnes*, it climbed from roughly 20% of patients in the late 1970s to a peak of 64% by the late 1990s — and modern meta-analyses show macrolide resistance still rising, from ~10% in 2008 to ~44% in 2024. Resistance can emerge within eight weeks of topical monotherapy and spreads beyond the treated patient. Benzoyl peroxide is the exception: it kills by non-specific oxidation, so resistance has not meaningfully developed against it.

ANTIBIOTIC RESISTANCE IN C. ACNES OVER TIME



RECOVERY

It does not bounce back

After oral antibiotics, *Pseudomonas* blooms, *Streptococcus* stays elevated, and protective *Lactobacillus* remains depleted weeks after the course ends.

RELAPSE

"The rule," not the exception

Biofilm shelters the bacteria conventional actives cannot reach, so the reservoir re-seeds within weeks — recurrence after non-isotretinoin therapy is expected.

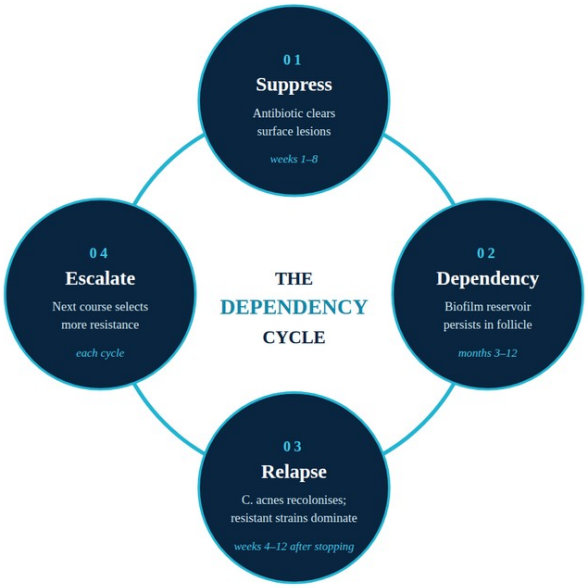
Sources: Dessinioti & Katsambas 2022; Platsidaki & Dessinioti 2018; Zhu et al. 2025; Chien et al. 2019; Coenye et al. 2021; Bagatin & Costa 2020.

THE LONG GAME

The dependency cycle

Conventional therapy suppresses free-floating bacteria but cannot penetrate the biofilm sheltering *C. acnes* inside the follicle. The result is a self-perpetuating loop: clearance, dependency, relapse, and escalation — each cycle selecting for more resistance and deeper dysbiosis.

WHY CONVENTIONAL TREATMENT BECOMES SELF-PERPETUATING



THE MECHANISTIC OPENING

An enzyme that **dismantles the biofilm scaffold without killing the bacteria** disperses *C. acnes* biofilm almost completely in vivo while leaving cells viable — exposing them to immune clearance and competitive displacement rather than driving a resistance arms race. **Removing the structure beats escalating the dose.**

Sources: Kayiran et al. 2020; Cavallo et al. 2022; Coenye et al. 2021; Bronnec et al. 2022; Kaplan et al. 2025.

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SECTION THREE · THE GLOBAL AMR CRISIS

Acne's hidden public-health problem

Acne prescribing is not a private matter. Skin conditions account for around 8% of primary-care antibiotic prescriptions — inside a resistance emergency measured in millions of lives.

THE GLOBAL AMR CRISIS

A crisis measured in millions

Bacterial antimicrobial resistance was associated with an estimated **4.95 million deaths in 2019**, of which 1.27 million were directly attributable — concentrated in lower-resource settings, and forecast to climb toward 8.2 million associated deaths a year by 2050. *C. acnes* resistance is now a global phenomenon with sharp regional contours, dominated by macrolide resistance across Asia.

Region	Key resistance finding	Source
Global pooled (2025)	Erythromycin 29% · clindamycin 22% · doxycycline 2.4%	Zhu et al. 2025
Europe (historical)	Any-antibiotic resistance up to 94% (Spain), ~75% (Greece)	Platsidaki & Dessinioti 2018
China	Clarithromycin ~77%; azithromycin ~55% (highest globally)	Zhu et al. 2025
India	Macrolide-dominant; ~25% multidrug-resistant isolates	Bhadade et al. 2026
Indonesia	Macrolide resistance up to ~60%	Zhu et al. 2025

FROM PREFERENCE TO PRIORITY

Guidelines now insist that systemic antibiotics be limited to the **shortest effective course** (ideally ≤3–4 months), never used as topical monotherapy, always paired with benzoyl peroxide, and transitioned to non-antibiotic maintenance. A credible non-antibiotic mechanism is an answer to a defining health challenge — not just a differentiator.

Sources: Murray et al. 2022; GBD AMR Collaborators 2024; Zhu et al. 2025; Zhang et al. 2023; Reynolds et al. 2024; Layton et al. 2018.

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SECTION FOUR · WHAT "ANTIBIOTIC-FREE" REALLY MEANS

The regulatory and commercial reality

“Antibiotic-free” and “antiseptic-free” are powerful phrases — but they carry a nuance that decides whether a product is a cosmetic or a drug.

REGULATORY & COMMERCIAL

Mechanism is positioning

Across the US, EU and Singapore, the line between a cosmetic and a drug turns on **intended use and mechanism**, not ingredient labels. The FDA classifies benzoyl peroxide and salicylic acid as over-the-counter acne *drug* actives — so a product containing them is a drug even when labelled "antibiotic-free." The EU Biocidal Products Regulation captures anything that controls microbes "by means other than mere physical or mechanical action" — which is precisely the carve-out a physical biofilm-removal mechanism can occupy.

THE TRAP

Antibiotic-free ≠ non-drug

Removing antibiotics addresses only one dimension. A non-antibiotic antimicrobial that kills bacteria or claims to treat disease still lands in drug — or biocide — territory.

THE WHITE SPACE

Physical removal, supported claims

A mechanism that **disperses** rather than kills, paired with disciplined "supports a balanced microbiome" language, occupies the clearest cosmetic pathway available.

THE STRATEGIC TENSION

The most recent translational review names **regulatory clarity** as a leading barrier for next-generation acne actives. The more powerfully a product demonstrates lesion reduction, the more it risks being pulled into drug classification — so the resolution is as much mechanistic as legal.

Sources: US FDA cosmetic/drug guidance & OTC Monograph M006; EU Regulation 1223/2009; EU BPR 528/2012; HSA Singapore; Mustaffa et al. 2026.

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SECTION FIVE · THE LYSIS PROBLEM

When killing bacteria makes things worse

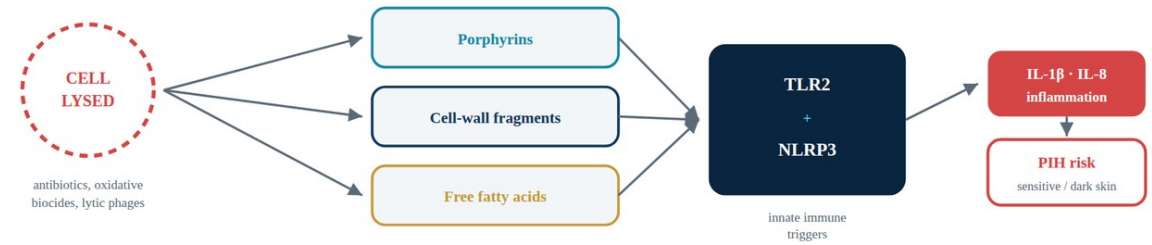
Killing a bacterium does not make its contents disappear. It releases them — a burst of inflammatory cargo that the skin must absorb.

THE LYSIS PROBLEM

The bomb inside the cell

When *C. acnes* is lysed — by antibiotics, oxidative biocides or lytic phages — it releases a bolus of **porphyrins, cell-wall fragments and free fatty acids**. Each is an established inflammatory trigger: porphyrins activate the NLRP3 inflammasome; cell-wall fragments ignite TLR2. Medicine has a name for the synchronised release of bacterial contents after killing — the Jarisch–Herxheimer reaction — and the same TLR2 biology applies to the skin.

WHAT KILLING RELEASES — AND WHAT DISPERSAL AVOIDS



PHYSICAL DISPERSAL — the cascade never fires

Cells stay intact · porphyrins remain contained · no TLR2 / NLRP3 burst · lower inflammatory and pigment risk.

WHO PAYS THE PRICE

For sensitive and **pigmentation-prone skin**, this inflammatory burst is not trivial: the cytokines that follow drive post-inflammatory hyperpigmentation — marks that can outlast the lesion by months. A non-lytic approach keeps the cargo contained.

Sources: Spittaels et al. 2021; Kim et al. 2002; O'Neill et al. 2019; Farfán et al. 2022; Nau & Eiffert 2002; Sangha 2021.

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SECTION SIX · THE NEW PARADIGM

Physical removal, not chemical warfare

Assemble the evidence and a coherent direction emerges — one that reframes what an acne active should be designed to do.

THE NEW PARADIGM

Restore, don't eradicate

Acne is a disorder of **balance and persistence**, not bacterial number. The load of *C. acnes* is similar in clear and acne-prone skin; what differs is the loss of phylotype diversity, the entrenchment of biofilm, and the inflammation that follows. A physical-removal paradigm answers each liability at once — without selecting for resistance, sparing the barrier and commensals, dismantling the relapse reservoir, and avoiding the lysis-release burst.

TWO PHILOSOPHIES, FIVE LIABILITIES

LIABILITY	KILL	REMOVE
Resistance selection	High pressure	No pressure
Skin barrier	Disrupted / dried	Spared
Microbiome	Broad collateral loss	Preserved, selective
Biofilm reservoir	Left intact, seeds relapse	Dismantled
Lysis inflammation	Contents released	Cells stay intact

AN HONEST FRAMING

This is a matter of **direction, not displacement**. Benzoyl peroxide remains a resistance-neutral workhorse, and the confirmatory long-term human trials for selective biofilm removal are still to be run. But across tolerability, resistance, stewardship, regulation and inflammatory safety, the weight of mechanism points the same way.

Sources: Dréno et al. 2020 & 2024; Mias et al. 2023; Coenye et al. 2021; Bronnec et al. 2022; Reynolds et al. 2024; Gamal et al. 2025.

IN CLOSING

Seven things to carry forward

1. **Acne is dysbiosis, not overgrowth.** Pathology tracks the loss of microbial balance and biofilm persistence — not the total count of bacteria.
2. **Every conventional active has an ecological cost.** Antibiotics drive resistance; benzoyl peroxide is resistance-neutral but barrier-disruptive; all leave biofilm largely intact.
3. **Recovery is incomplete and relapse is the rule.** The microbiome does not fully rebound, and recurrence follows when the reservoir survives.
4. **Acne antibiotics are a public-health issue.** Against millions of AMR deaths, stewardship now demands short courses and non-antibiotic maintenance.
5. **"Antibiotic-free" is not "non-drug."** Classification turns on mechanism and claims; physical removal is the clearest route to cosmetic positioning.
6. **Killing bacteria can worsen inflammation.** Lysis releases porphyrins and cell-wall fragments that trigger inflammation — a real liability for sensitive and pigment-prone skin.
7. **The future is restoration, not eradication.** Selective, non-lytic biofilm removal addresses resistance, barrier, dependency and inflammation at once.

> *The question is no longer how thoroughly can we kill? — but how intelligently can we restore?*

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Why Killing Bacteria Is Not the Answer

A public educational piece grounded in peer-reviewed evidence (2015–2026) and primary regulatory sources. Statements describing selective biofilm-removal benefits reflect mechanistic and preclinical evidence and are not claims of demonstrated clinical superiority. No product or brand claims. Not medical or regulatory advice.

SELECTED SOURCES

Reynolds et al., JAAD 2024 · Murray et al., Lancet 2022 · GBD AMR Collaborators, Lancet 2024 · Coenye et al., Biofilm 2021 · Cavallo et al., Sci Rep 2022 · Chien et al., JAMA Dermatol 2019 · Zhu et al., Front Microbiol 2025 · Dessinioti & Katsambas 2022 · Spittaels et al., iScience 2021 · Farfán et al., PeerJ 2022 · Bronnec et al., Front Cell Infect Microbiol 2022 · Mustaffa et al., AAPS PharmSciTech 2026. Full reference list available in the companion document.

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