Getting Patients Involved in the Cold Chain

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temperature control beyond the last mile

Temperature management right down to point-of-use is an elusive goal. Here is one way of ensuring product safety after an OTC or self-administered pharma product gets into the hands of a final consumer or care giver.

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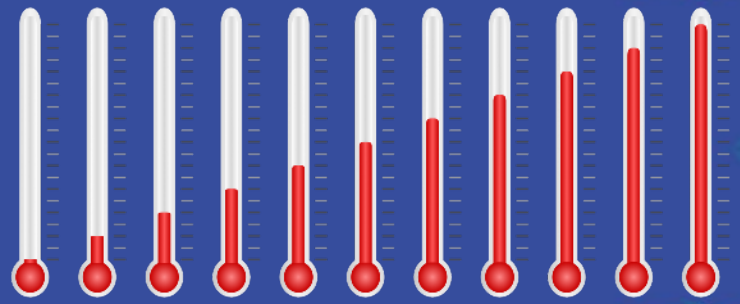
What is a temperature excursion?

"A temperature excursion is the deviation from the labelled storage condition of a product for any duration whether during transportation or distribution. Studies indicate that if there is exposure of product or intermediate beyond specified environmental limits for substantial time, there shall be generation of impurities as a result of product degradation. Such degradation products are not only regarded as undesired but also shall have adverse reaction to the patient's health."

Temperature Excursion Management: A novel approach of quality system in pharmaceutical industry, Kumar, Jha, Saudi Pharmaceutical Journal, Feb 2017

Hot & Cold Excursions



Spot the Difference?

Frequency

of temperature excursions

“Temperature excursions during transport are not rare events.

Excursions happen at a frequency of 1% - 5% of transport events.

This places transport as one of the least reliable pharmaceutical processes”

Last year the UK’s MHRA reported that 9% of ‘Major Deficiencies’ encountered during audit inspections related to Temperature Control (storage) and 13% to Transportation.

"Handling Temperature Excursions and the Role of Stability Data", C. Ammann, Pharmaceutical Outsourcing Sep 2013

Cold Chain Failure

The World Health Organization has reported that in a vaccine management study carried out in more than 70 countries between 2010 and 2012, as few as 29% of countries met its minimum recommended standards for temperature control".

Where do Temperature Excursions Occur?

"Research shows that most temperature excursions occur within a mile of a shipment's destination — meaning we need technology capable of monitoring a temperature-controlled shipment from packing through transport, storage and delivery".

"The evolution of temperature-controlled transport - how innovation overcomes the biggest challenges in cold chain supply", S. Lee, World Courier

Point of Consumption PoC

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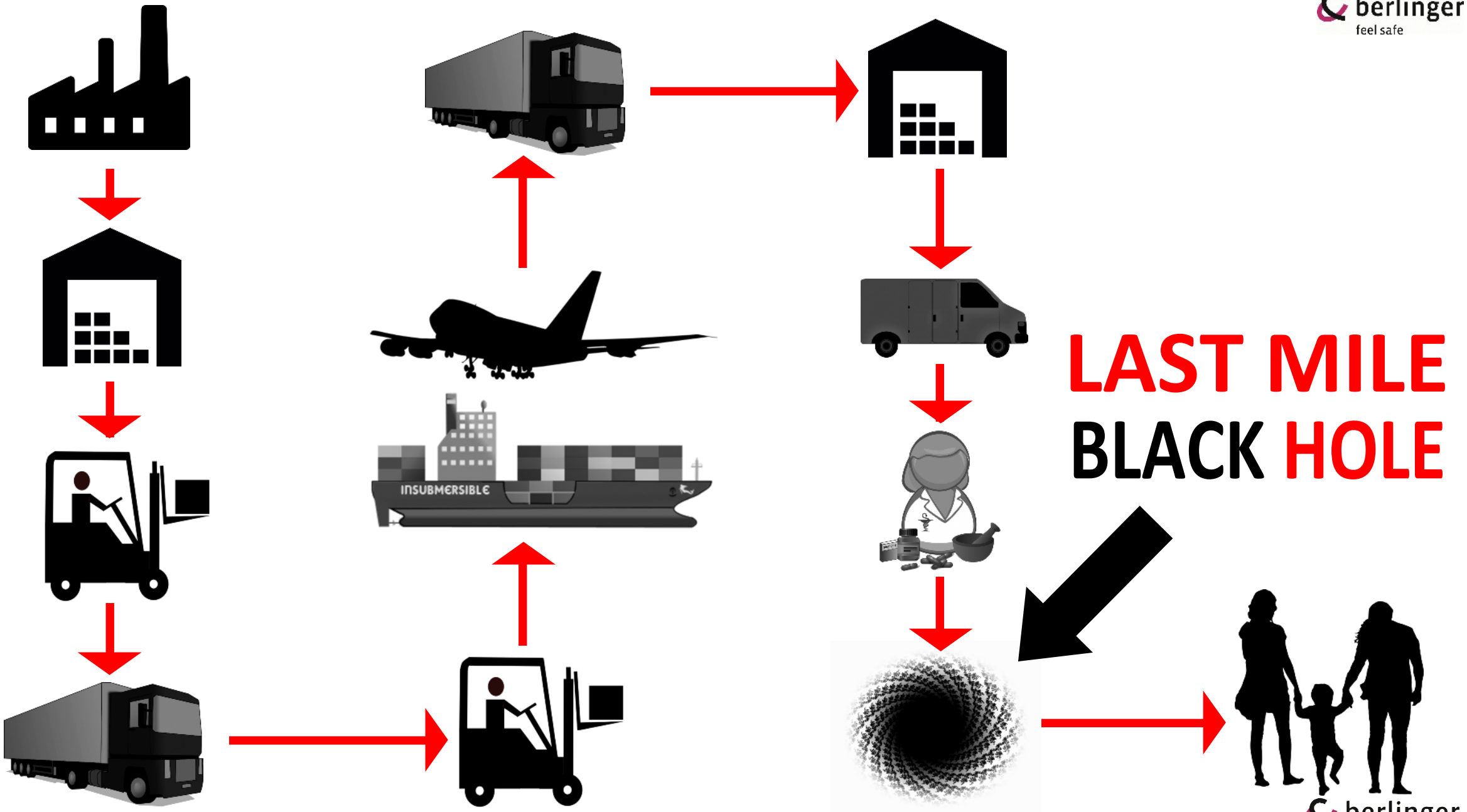
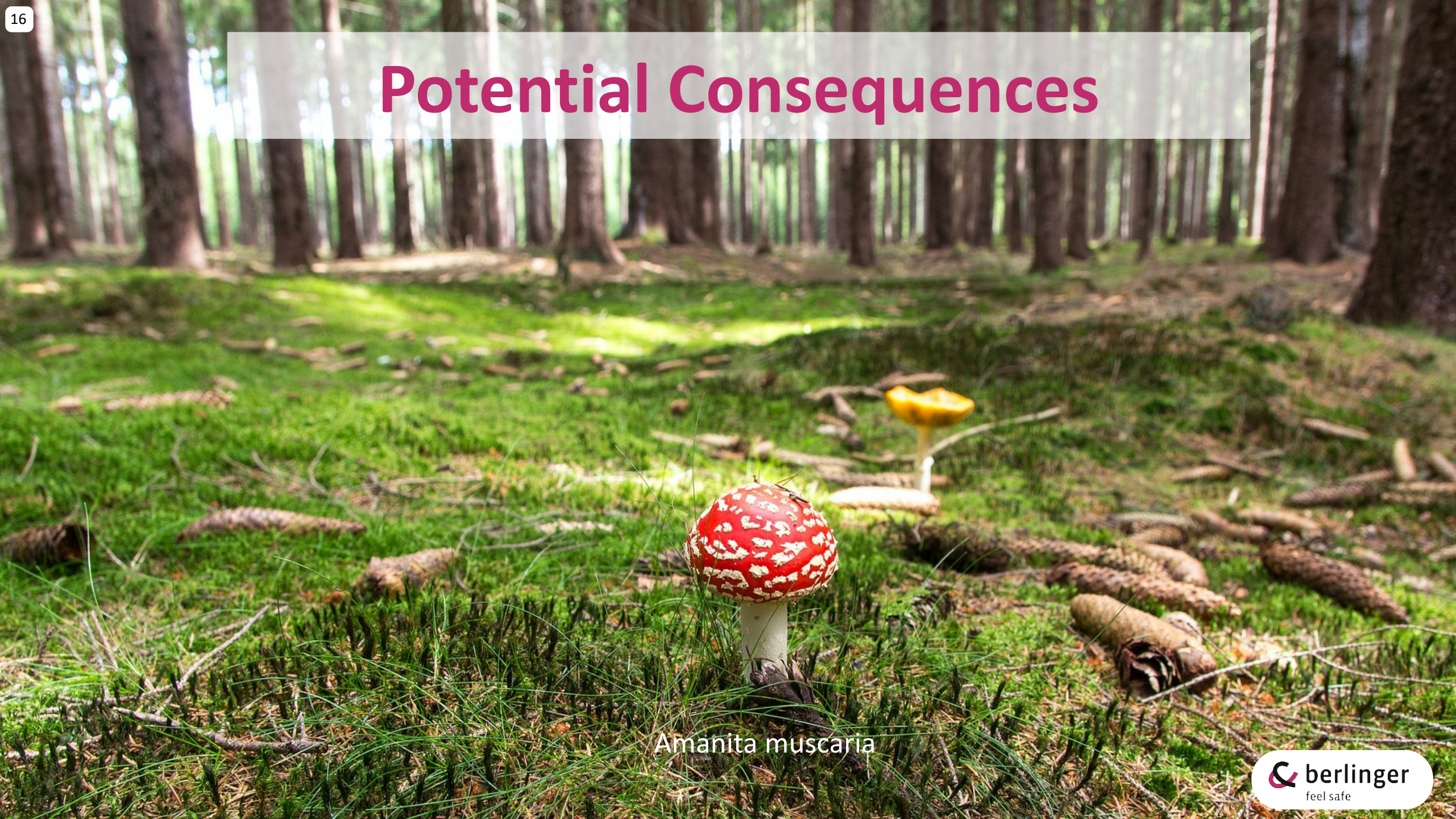

INSUBMERSIBLE
LAST MILE
BLACK HOLE

Domestic Medicine Management

Consumer Competency

Potential Consequences



Amanita muscaria

Real-life storage conditions

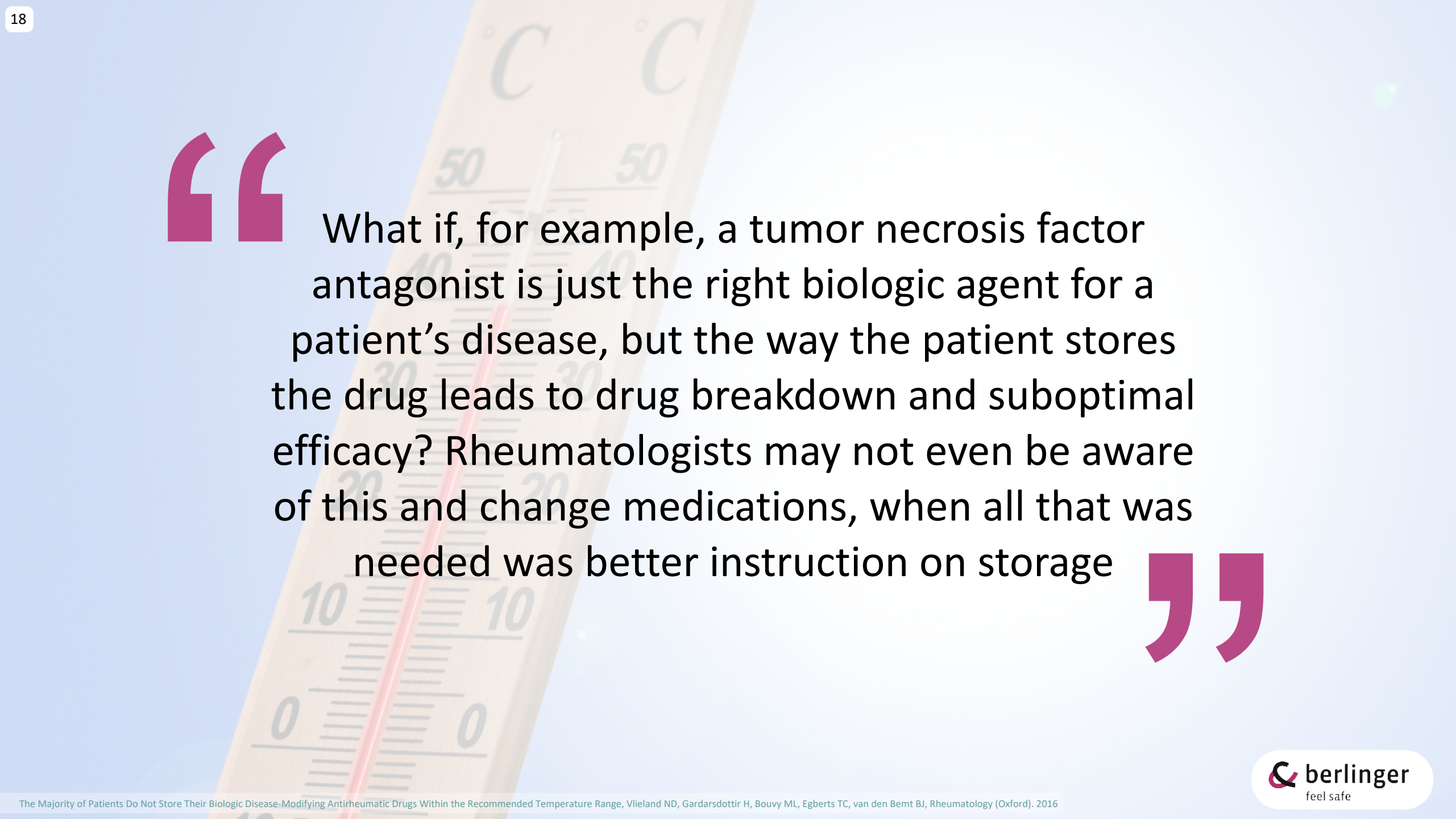
2016 Study

255 PARTICIPANTS:

Only 17 (6.7%) stored medication within recommended temperature range.

24.3% had stored their medication for more than 2 hours outside of the recommended range.

The Majority of Patients Do Not Store Their Biologic Disease-Modifying Antirheumatic Drugs Within the Recommended Temperature Range, Vlieland ND, Gardarsdottir H, Bouvy ML, Egberts TC, van den Bemt BJ, Rheumatology (Oxford). 2016



> What if, for example, a tumor necrosis factor antagonist is just the right biologic agent for a patient's disease, but the way the patient stores the drug leads to drug breakdown and suboptimal efficacy? Rheumatologists may not even be aware of this and change medications, when all that was needed was better instruction on storage

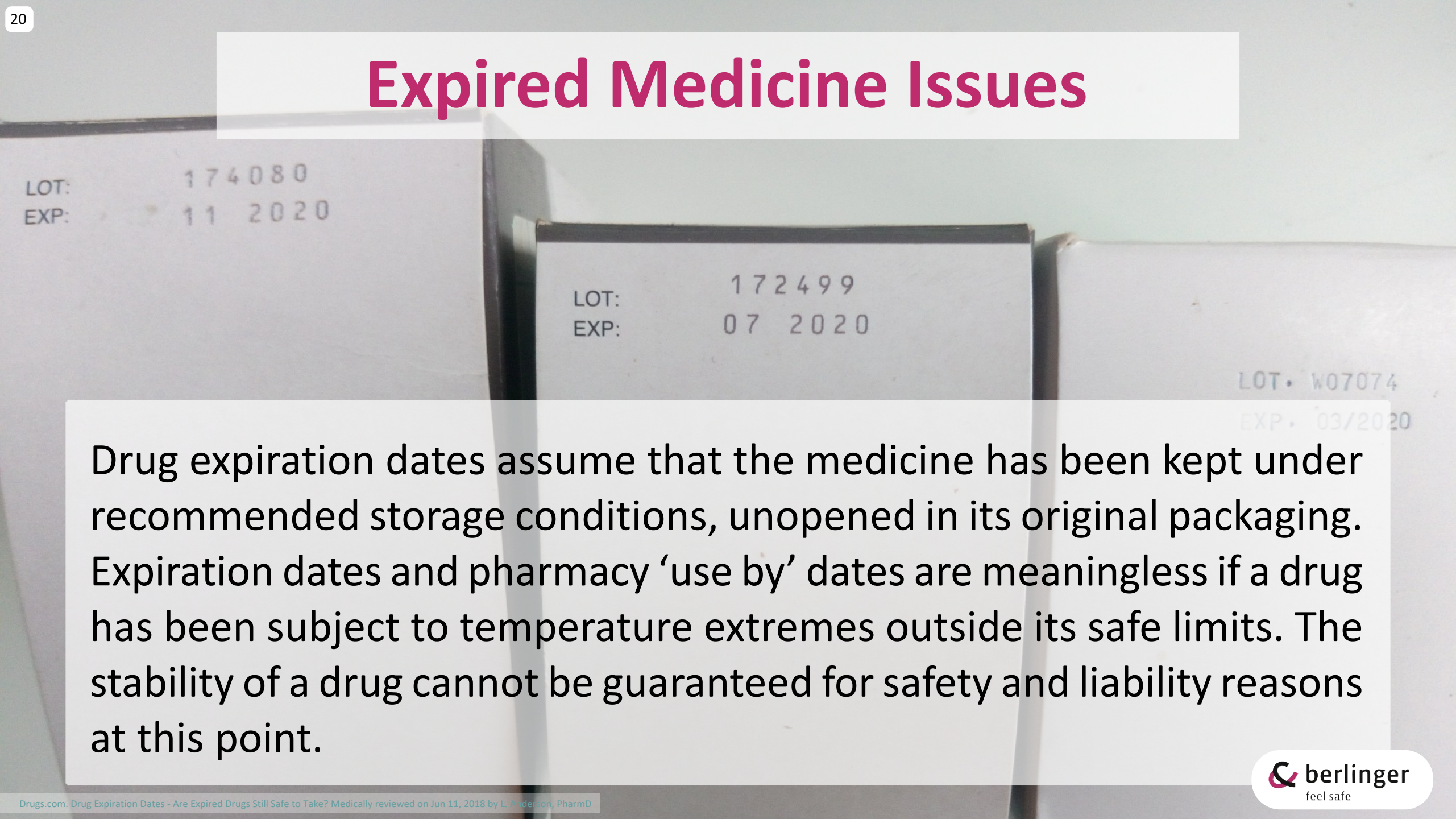
The Majority of Patients Do Not Store Their Biologic Disease-Modifying Antirheumatic Drugs Within the Recommended Temperature Range, Vlieland ND, Gardarsdottir H, Bouvy ML, Egberts TC, van den Bemt BJ, Rheumatology (Oxford). 2016

Label and Insert Difficulties

There are about 1.5 million preventable medication errors each year, according to a report from the Institute of Medicine. Roughly one-third of those mistakes occur outside of hospitals, where patients must rely upon their own ability to follow the instructions on their medication containers. Half of adults in outpatient settings misunderstand at least some of the instructions on a drug's label.

Institute of Medicine "Study Finds Many Patients Don't Understand Prescription Medicine Labels." Science Daily, 30 Nov 2006

Expired Medicine Issues



Drug expiration dates assume that the medicine has been kept under recommended storage conditions, unopened in its original packaging. Expiration dates and pharmacy ‘use by’ dates are meaningless if a drug has been subject to temperature extremes outside its safe limits. The stability of a drug cannot be guaranteed for safety and liability reasons at this point.

Drugs.com. Drug Expiration Dates - Are Expired Drugs Still Safe to Take? Medically reviewed on Jun 11, 2018 by L. Anderson, PharmD

Example - Insulin

28 days at 30°C

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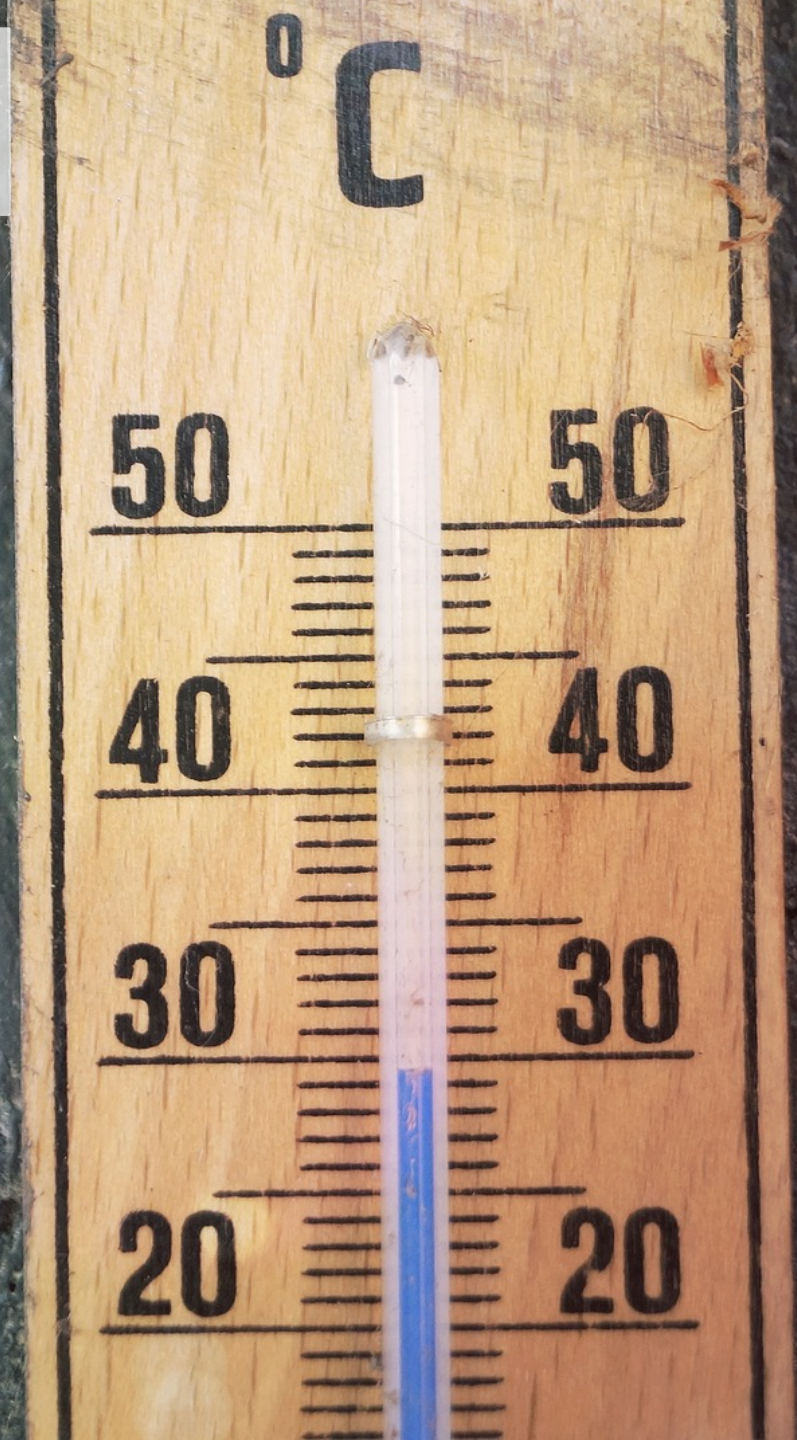
Potency decrease of 18% compared to correct storage at 5°C



Progressive and irreversible degradation

Keeping the Cold Chain Cold / Vaccine Supply Chains×Reaching the Final 20 Policy Paper Series. Seattle: VillageReach; 2014

Discarded Medicines

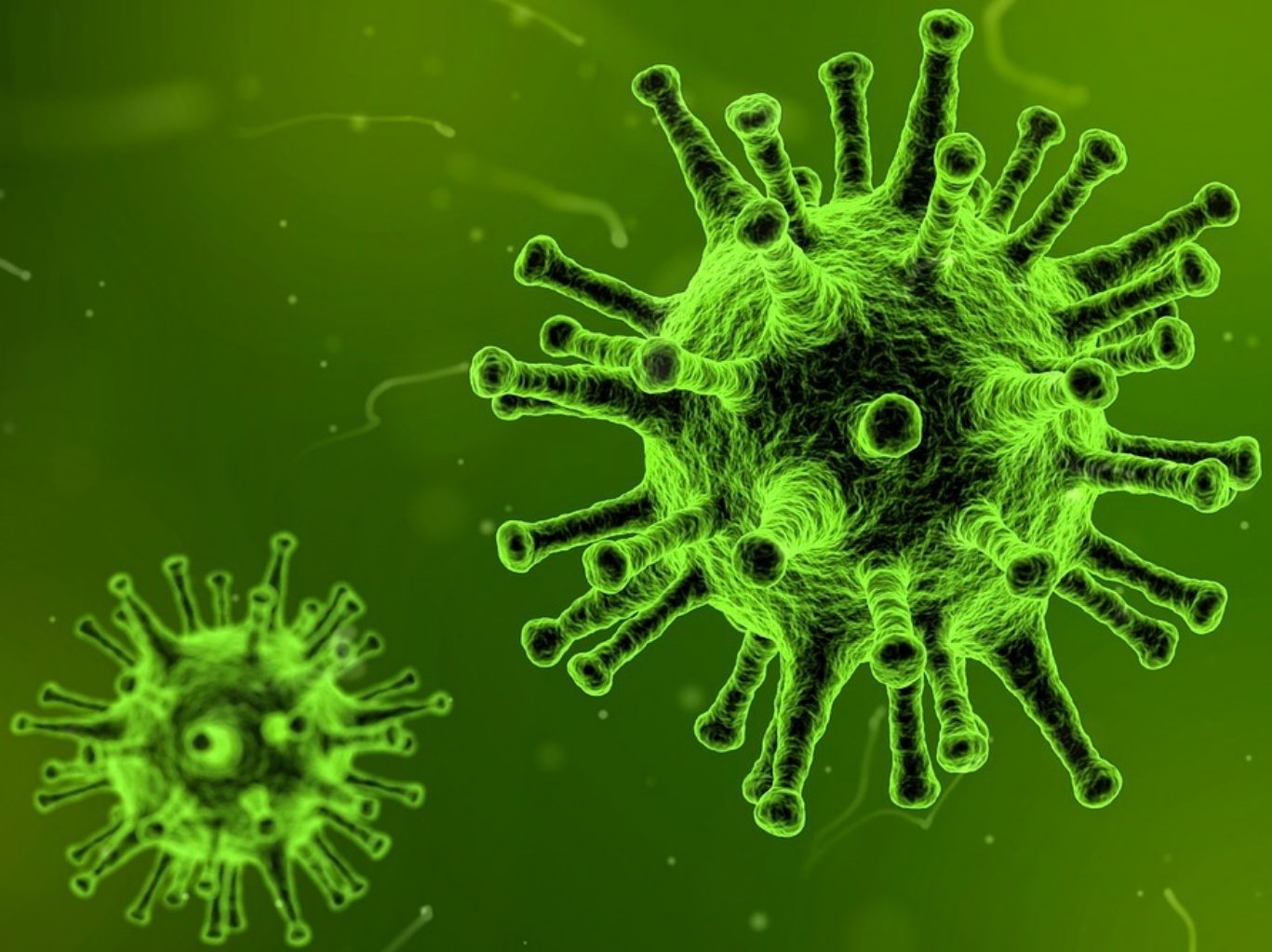
An estimated $10bn worth of pharma products are thrown away each year. In fact US hospitals alone are reported to discard over $800 million in drugs annually.

How much medicine does healthcare throw away each year?', B Blake, SCM World, Jun 14, 2016

Increasing Importance of Last Leg

- Increasing direct mail distribution of medicines
- Specialty medicines more personalised, expensive, and environmentally sensitive
- New remote diagnosis systems further isolating patients from the health system
- Introduction of outcome-based drug payment models
- Switch from curative to preventative treatments e.g. statins instead of heart surgery
- Increasing continuous consumer health monitoring and adherence esp. phone apps
- Growth of auto-replenishment systems such as 'Amazon Dash'
- Huge drug wastage levels at both health facility and consumer levels
- High incidence of risky consumption of drugs stored incorrectly and too long
- Increasingly rigorous GDP adherence requirements and inspection diligence

Rise of Biologics



Personally-Tailored Medicines

Supply Chain Complexity

ORIGIN

Manufacturer | Trucker | Freight Forwarder | Airline Cargo Handler | Airline

TRANSFER

Airline | Airline Cargo Handler | Airline

DESTINATION

Ariline | Airline Cargo Handler | Regulatory Authority | Trucker | Freight Forwarder | Trucker | Consignee

Low risk | Medium risk | High risk

Temperature excursion risk points in pharma air-freight

Human Error

Escalating Medicine Costs

Mail Delivery of Medicines

Solar Exposure

The interior temperature of a black mail box with full sun exposure was monitored for a 4-month period. The maximum temperature of 136°F (58°C) was recorded in an ambient temperature of approximately 101°F (38°C). The maximum interior versus exterior temperature difference was approximately +31°F (+17°C)

"Summer of 1995 Mailbox Temperature Excursions in St. Louis," J.C. Black and T.P. Layloff, Pharmacopeial Forum, 1998, 22, 3305.

Mounting Regulatory Oversight

Regulatory bodies - FDA, EMA, MHRA etc. - must ensure that medical products are “safe, effective, and appropriate for their intended use”

Centers for Disease Control and Prevention, Epidemiology and Prevention of Vaccine-Preventable Diseases, 13th Edition April, 2015

Rules of State of Georgia Board of Pharmacy

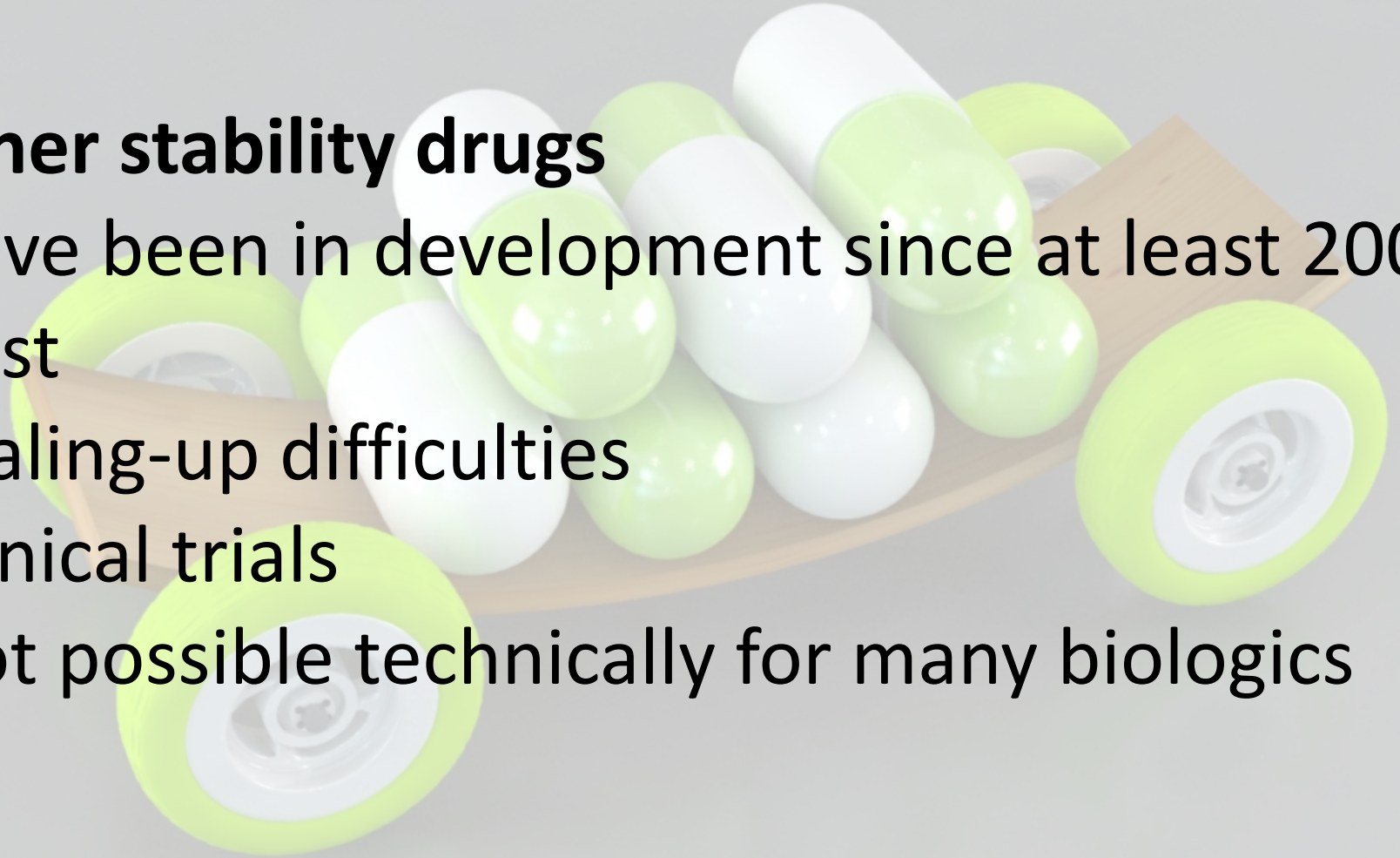
Chapter 480-48 DELIVERY BY MAIL ORDER

(3) “A mail order pharmacy shall ensure that all prescription drug order medications are delivered to the patient in accordance with standards of the drug manufacturer's temperature standards as set by the Food and Drug Administration (FDA).Pharmacy shall insure integrity of any drug requiring temperature control other than "room temperature storage" that is delivered by mail order by enclosing in each medication's packaging a USP-recognized method by which the patient can easily detect improper storage or temperature variations.”

Tomorrow's Solution?

Higher stability drugs?

Higher Stability Drugs?



Higher stability drugs

- Have been in development since at least 2004
- Cost
- Scaling-up difficulties
- Clinical trials
- Not possible technically for many biologics

Today's Solution

Miniaturised Temperature Indicators

Extending responsibility for greater temperature management in the direction of the final consumer

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Technical Requirements

- small size
- low weight
- low cost
- low-power source
- high reliability
- high accuracy
- high ease-of-use
- pre-calibrated
- high-contrast alert for visually impaired

Limitations

- need to be correctly inserted/positioned/attached
- need to be tested/approved/qualified

Cost Implications

Of course it will cost money to render drugs safer at point of use.

However, the real cost of cutting corners on temperature management relates to the potential for lost lives or poor therapeutic outcomes as a result of compromised medicines.

The Mini-tag Indicator from Berlinger

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Basic Characteristics

Green = OK Red = Not OK

Accuracy ±0.5°C

Up to 3 separate alarm limits can be programmed

Tiny size
- just 1.375" x 1.0" x 0.125"

Operating life of up to 3 years

Miniaturised electronics fully encapsulated in robust casing

Measures between -25°C and +55°C

Measurement intervals of 3, 5 or 10 minutes

Tiny weight - just 0.141 oz

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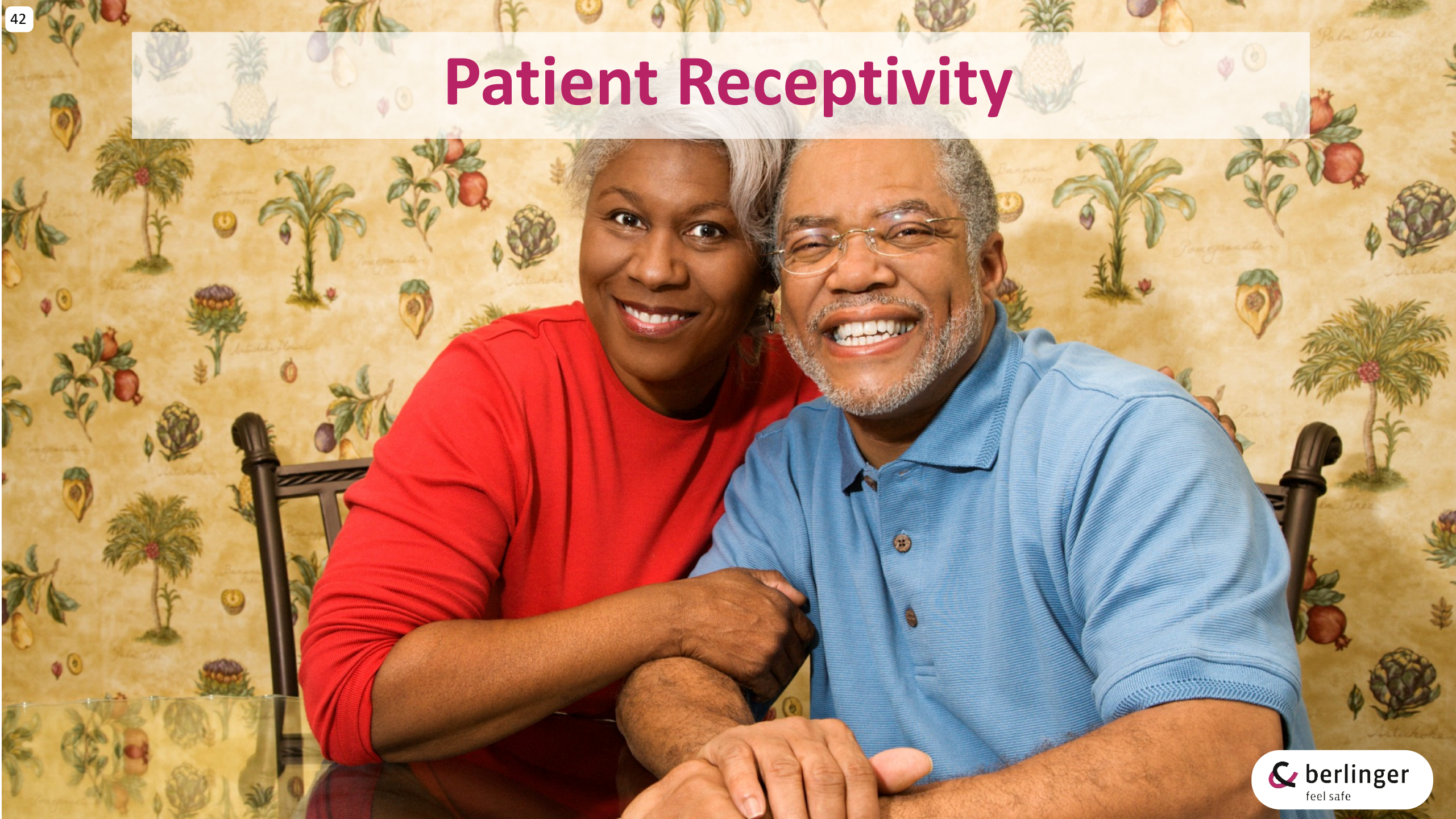
Patient Responsibility

Patient Receptivity



Attention Shift to Point of Consumption

In the United States alone, 31 percent—or $161.6 billion - of the food supply goes uneaten.

Keeping Food Out of the Landfill, Harvard Food Law and Policy Clinic, Oct 2016

Building Consumer Trust

Less than one quarter of Americans have much confidence in the healthcare system

Public Trust in Physicians — U.S. Medicine in International Perspective - Blendon, Benson, Hero; N Engl J Med 2014

Standalone Device

Not ‘track & trace‘

Not harvesting consumer data

Not affected by EU GDPR regulations

Not affected by the Health Insurance Portability and Accountability Act of 1996 (HIPAA)

Conclusions

- How many drugs are thrown away due to being judged unfit for human consumption at point of use?
- How many drugs are consumed that are outside the official margins for safety?
- These are serious issues that to a large degree can be addressed through equipping individual medicine containers with inexpensive temperature indicators that are accurate, reliable and easy-to-use.
- Such a safety feature will reduce waste, improve curative outcomes and increase consumer confidence. It will also grant the drug supplier with a huge market differentiator and positive brand reinforcement.

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