

Material Variability – How Much?

A Plastics Manufacturer's Perspective

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IPAC-RS Materials Forum
September 13+14, 2009



Content

- History of polyolefins producers
- Current practices
- Future perspective



Introduction

This presentation is designed to focus only on LyondellBasell's experiences and does not represent the views of the industry



History: LyondellBasell and its predecessors

- 1950s: Industrial-scale PE production (Philips process, Ziegler process); development of Ziegler-Natta catalysts for PP
- 1960s: PE and PP plants in production across the globe; polyolefins become competitive commodity plastics
- 1970s: First production of grade used in healthcare at Wesseling, Germany: PE3020D used in IV bottles
- 1990s: First conceptual approaches to healthcare applications: Specific guarantees (e.g. no change of formulation) for selected products and customers (Montell)
- 2002: Basell became first polyolefins producer to launch dedicated portfolio of polyolefins for healthcare applications – *Purell*



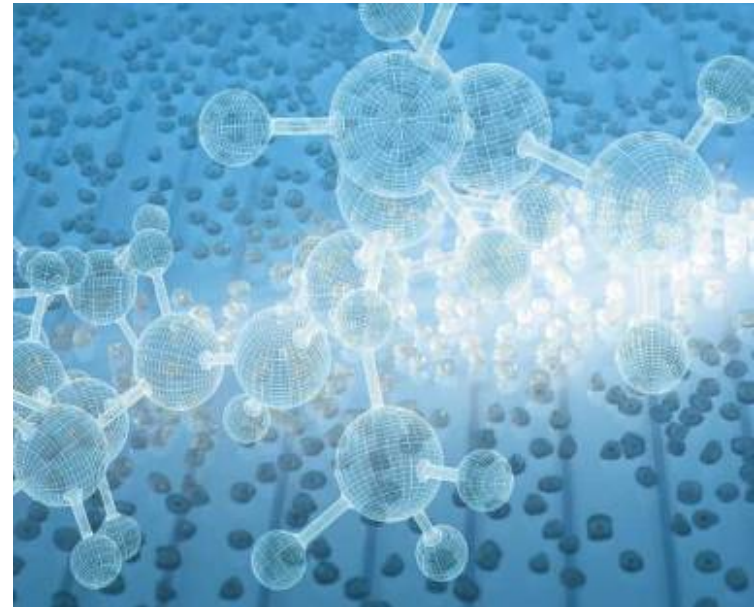
History: The polyolefins industry

- Strong legacy of commodity production, with key drivers
 - Volume
 - Cost efficiency
- ➔ A paradigm shift in thinking is required to produce small volumes under exceptional quality standards – which is why very few producers have adopted the concept on a global basis



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Current practices

- Leading polyolefins producers offer dedicated range of products for healthcare applications
 - Leading pharmaceutical and medical device companies focus on...
 - quality
 - safety
 - patient convenience
- ...in a holistic approach, comprising everything from manufacturing, packaging and supply chain to patient care

Cornerstones of LyondellBasell's *Purell* principle

- **No change of formulation – Long-term supply**

We keep the formulations of *Purell* resins constant, unless changes are required by law or unavoidable for operational reasons. We then give two years notification of changes or reasonable safety stock.

- **Single sourcing**

We deliver *Purell* resins constantly from the same plant to ensure consistency

- **Back-up plants concept**

To further enhance security of supply, we offer back-up plants for the supply of select *Purell* resins

- **Compliance with regulatory requirements**

Certificates for USP, Ph.Eur. or ISO10993 compliance; DMFs filed

Differences are in the details

As a pharmaceutical sponsor, would you like to better understand if this paradigm shift in thinking has really occurred?

- Senior management commitment to low volume, high cost products?
- Auditable local procedures available and fully implemented in plants?
- What degree of 'pharmaceutical thinking' has been established in these procedures?
- Are appropriate risk management procedures in place and observed?
- Is appropriate documentation provided?
- Do your suppliers match your global outreach?
- Do the teams involved (especially technical services) have sufficient expertise beyond their technical education?

LyondellBasell guidelines

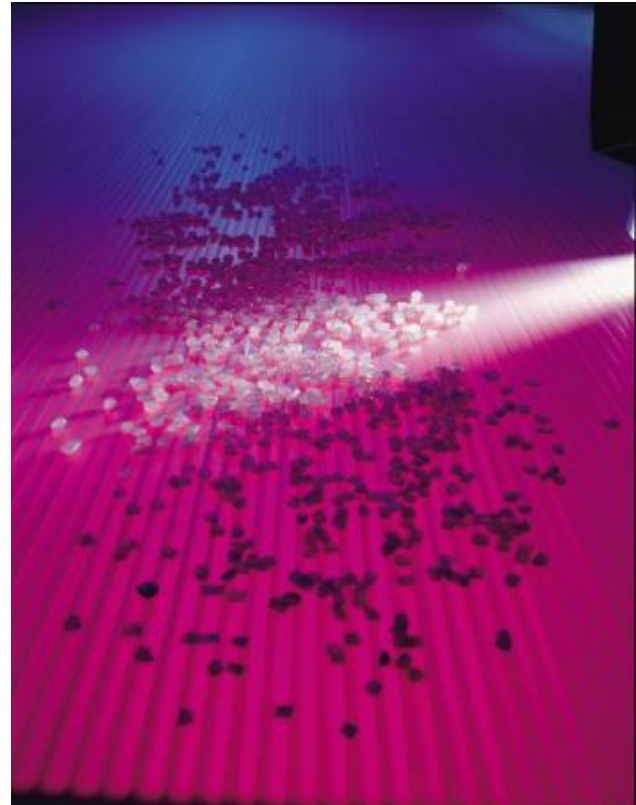
Based on our experience with products used in pharmaceutical packaging and medical devices, we have developed a **Global Medical Procedure** that

- is binding to all LyondellBasell plants producing *Purell* products
- covers all stakeholders (manufacturing, supply chain, business management, sales, technical service, regulatory, etc.)
- reflects the spirit of central GMP standards: awareness, change control and documentation



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Future opportunities and key issues

- Improve communication across supply chain



- Establish regular forums/workshops
- Team up with ELSIE, PolymerForum, etc.



- Jointly define key product criteria (such as general L&E testing)
- Better understanding of capabilities and limitations (conduct educational sessions on polyolefin production)

Future opportunities and key criteria: Definitions

Material Variability

Due to the nature of polymerization even the same product manufactured in the same plant can be different in different batches. The range of this “difference” is identified in the **product specifications** and refers to physical parameters (e.g., density) and chemical composition.

Product Change

A product change is any change in the chemical composition of raw materials (e.g., additives), the production plant, a product’s regulatory status, etc. – beyond what has been identified in the product specifications.

Communication

A product change must be communicated to the sponsor, ideally as a pre-notification. It is important to make sure the material producer is aware of the sponsors that will be affected.

Confidentiality

Depending on the details that need to be exchanged, it might be necessary to establish confidentiality.

What if a change becomes necessary?

- Any product change must be *approved by business management*, according to our Medical Procedure. During this review process, we contact our (key) customers and discuss the change with them.
- Issue: Will we be informed if our additive suppliers change their product?
- In case of a product change, we inform customers about the implementation of the change, including the notification on the two year transition period.
- After one year, we liaise with customers to define the “last call” to be produced within the coming year.

Future opportunities and questions

- If we are to look at L&E – what exactly needs to be measured?
- Can we achieve a common approach among all sponsors?
- How can duplicate/multiple testing be avoided? Note that a raw material supplier can only provide a ‘starting point’ and cannot comment on any subsequent step such as converting, additive addition, pigment addition, etc.
- Is the definition of ‘product change’ comprehensive enough?
- How can we make sure everyone is informed on time?
- How can we ensure confidentiality?
- At which point in the decision-making process should information be disclosed?
- ...

Future opportunities: A proposal

- Establish a forum where representatives of the entire supply chain are present, such as raw material producers, converters, and sponsors
- This forum should
 - establish a mission to provide answers to the aforementioned questions
 - find a way of balancing the information required and the cost associated with generating it
 - observe rules to avoid any price or performance comparisons
 - consider liability issues and concerns

Future opportunities: A starting point

- PolymerForum, ELSIE initiatives are already in place/underway
 - Why not involve raw materials suppliers?
 - These workshops are very helpful!
- ➔ Let's change the traditional way of communicating - to the benefit of all, including the patients!

Thank you for your attention!



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