



The slide cover features a blue background with a yellow horizontal band. On the left, there is a photograph of laboratory glassware and a scientist. The PDA logo and tagline are in the top right. The title 'API Supply Chain Integrity' is in the yellow band. Below it, the subtitle 'Perspective from the Generic Medicines Industry' is in white. The speaker's name and dates are in the bottom left, and the EGA logo with the tagline 'Making Medicines Affordable' is in the bottom right.

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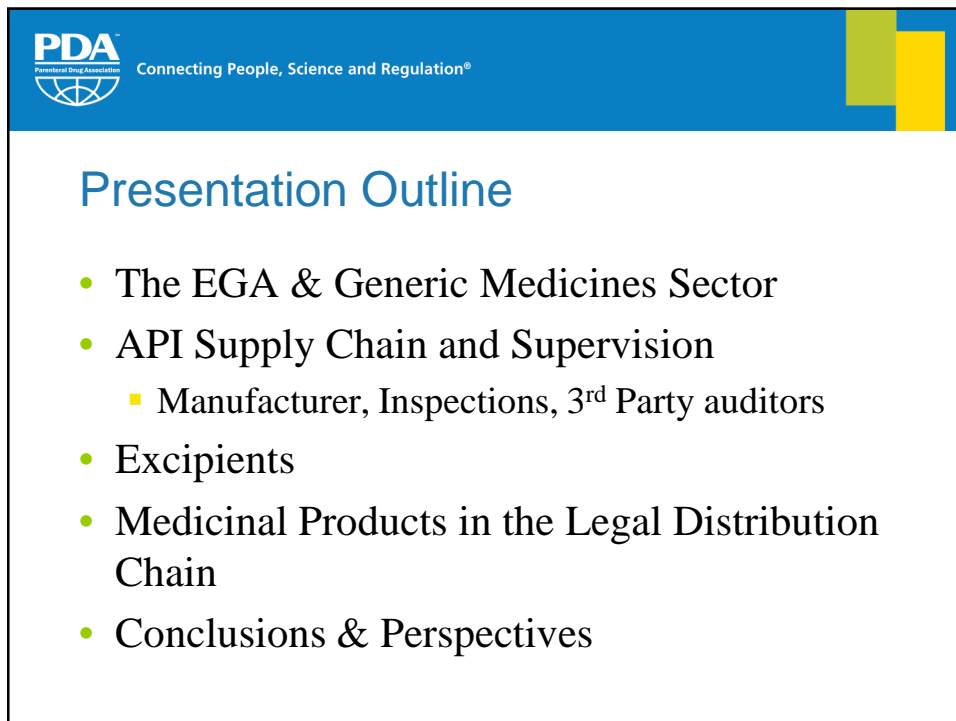
API Supply Chain Integrity

Perspective from the
Generic Medicines Industry

J. Maréchal-Jamil
Munich,
10-11 March 2009

EGA
Making Medicines Affordable

Photo courtesy of Texwipe



The slide has a blue header with the PDA logo and tagline. The main content is on a white background with a blue title and a bulleted list of topics. A decorative graphic of green and yellow squares is in the top right corner.

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Presentation Outline

- The EGA & Generic Medicines Sector
- API Supply Chain and Supervision
 - Manufacturer, Inspections, 3rd Party auditors
- Excipients
- Medicinal Products in the Legal Distribution Chain
- Conclusions & Perspectives



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Generic Medicines: Key to Healthcare Sustainability and Patient Care



- EGA represents over 700 companies in 34 European countries
- Generic medicines companies employ over 130,000 people in the EU
- Generic medicines account for nearly 50% of packs dispensed in the EU and 18% of pharmaceutical expenditure



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Generic Medicines: Key to Healthcare Sustainability and Patient Care



- Generic medicines bring savings of over €25 Billion per annum in the EU 27
- Generic medicines companies cover a full spectrum of pharmaceutical needs
- Generic medicines companies also undertake incremental innovation



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Generic Medicines Sector

- Very heterogeneous and diverse industry sector:
 - Large or medium-size portfolios
 - Global operations vs regional operations
 - Pharmaceutical development vs Licensing-in
 - API captive production vs API sourcing

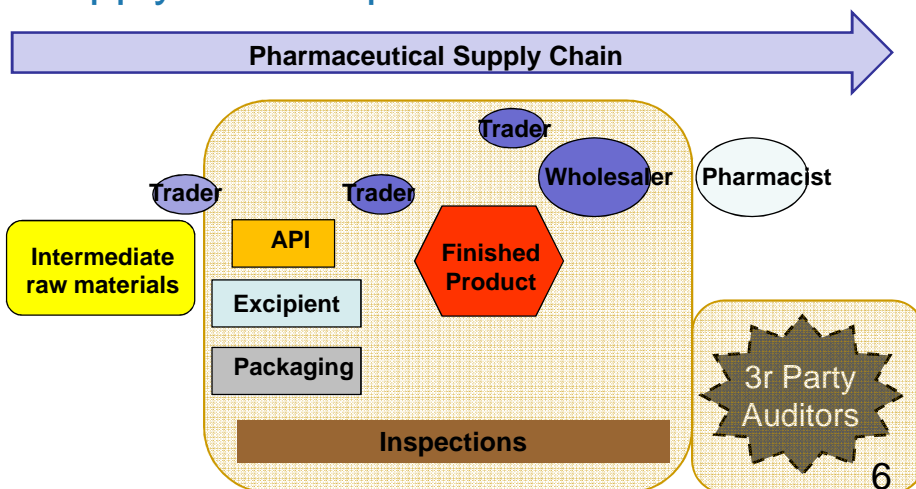
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Supply Chain Operators & Enforcement



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API SUPPLY CHAIN AND SUPERVISION:

- MANUFACTURER,
- INSPECTIONS,
- 3RD PARTY AUDITORS

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Key Elements for Supply Chain Integrity

- Adequate supervision of compliance to current standards
- Enforcement of legal provisions and corresponding contractual agreements

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Audits by Medicinal Product Manufacturers: Punctual Snapshots

- Regular supervision by audits
- Enforcement means by industry consists of commercial penalties
 - Strong driver provided there is a level playing field and Authorities enforcement



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Continued & Comprehensive Overview Beyond the Technical Agreement...

- Relationship with API manufacturers is an essential part of maintaining integrity
 - Direct and personal contact
 - Physical visits/audits
- Only guarantee for:
 - Uninterrupted and timely exchange of information
 - Continuous Quality Assurance



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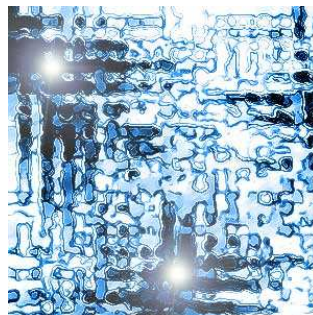
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Maintaining Supply Chain Integrity While Managing Change Control (1/2)

- MP Manufacturers need details of all changes to:
 - Assess the impact on MP and its intended use
 - Benefit vs Risk ;
Major, Minor, Other
 - Proceed with the variation procedure with adequate supportive information



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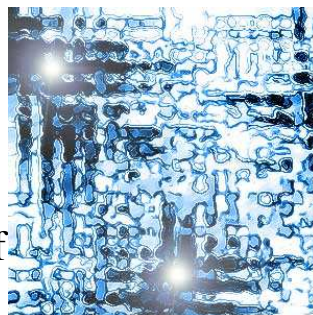
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Maintaining Supply Chain Integrity While Managing Change Control (2/2)

- Limited concerns when API production is captive
- API Sourcing: Importance of EU Regulatory system knowledge



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Product & Process Improvements Should Be Stimulated and Not Hindered

- Revision of the variation regulation will certainly benefit the industry and patients
 - ✓ ■ Allow for more product and process improvements
 - ✓ ■ Allow for smoother implementation of changes
 - ✓ ■ Allow for more affordable medicines



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EU Inspections

- ✓ • Efficient Quality Assurance Assessment (snapshot)
 - Particularly when unannounced
 - Means of enforcement: RA sanctions
 - eg, “until all concerns have been appropriately addressed”
- Risk-based approach to prioritisation
- ✓ • Transparency of the EU public repository:
- ✓ • EudraGMP database



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Enhanced Authorities Scrutiny Through International Inspection Cooperation

- ✓ • EU-FDA-TGA pilot programme
- ✓ • EC Proposal for the “Equivalence of Standards Concept”
 - Beyond the traditional MRA
 - Mid- and long-term perspective
 - Possibility for local inspectors to perform unannounced inspections



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Third Party Auditing

- EGA welcomes this option
- MP Manufacturer remain primary responsible: only the task is outsourced
- Open questions remain to be addressed:
 - Modalities of accreditation? Statute ?
 - Scope of audits?
 - Confidentiality ?
 - Guarantee of independence of auditors?



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EXCIPIENTS

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Pharmaceutical Excipients and GMP requirements

- The EGA supports a pragmatic and risk-based approach to GMP for excipients
 - ✓ ■ Specific or Novel excipient categories
- Any specific decision should carefully
 - Assess the risk of supply disruption
 - Ensure continuous access to medicines

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MEDICINAL PRODUCTS IN THE LEGAL DISTRIBUTION CHAIN

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Strengthening the Medicinal Product Supply Chain: Safety Features (1/2)

- EC proposal:
 - Implementation of safety features, for prescription medicines in the legal supply chain in relation to their risk of being counterfeited
- Counterfeiting is a behavioural problem
 - Safety features are only a 2^{ary} line of defence
 - They will not fully prevent falsified medicines from reaching patients

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Strengthening the Medicinal Product Supply Chain: Safety Features (2/2)

- If introduced, need for:
 - ✓ ■ Proven efficiency to improve patient safety
 - ✓ ■ Harmonised safety features in the EU & beyond
 - ✓ ■ Sustainable system in time
 - ✓ ■ Specific & well-defined risk-based assessment criteria
 - ✓ ■ Investments incurred to be proportionally distributed (ie, price of medicines concerned)

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Legal Medicinal Product Supply Chain: Other EGA considerations

- Open question remain:
 - What about regulating the internet at Community level ?
- EGA additional proposals
 - ✓ ■ EU Wholesaler's Licensing System Harmonisation
 - ✓ ■ Business with certified/licensed partners only



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Tackling Counterfeit and Substandard Medicines: EGA actions

- The EGA has been at the forefront of the fight against counterfeiting, taking an active role with different initiatives:
 - WHO IMPACT (2006, Anti-Counterfeiting Task Force)
 - GS1 Healthcare (2005, Global Coding Entity)
 - Council of Europe (2004)
 - European Healthcare Initiative (EAN 2001)

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CONCLUSIONS & PERSPECTIVES

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Conclusions (1/2)

- The Generic medicines sector is dedicated to continue building Quality in its Products
- Audits & Inspections of API manufacturers remain of primary importance
- New measures should
 - Establish benefits for patients
 - Be proportionate and cost effective



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Conclusions (2/2)

- However, GMP alone will not be the answer to fraud, intentional contamination or any other criminal or illegal behaviour !
- Safety features are only a 2^{ary} line of defence
 - 1^{ary} action : better enforcement, and criminal sanctions, as well as doing business with certified par




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Future Perspectives: EC Directive proposal:

- An opportunity to improve & enhance the current system
 - Clarified scope of applicability
 - Enhanced scrutiny for Authorities - cooperation
- Pragmatic:
 - Secures continued supply of quality medicines
 - While optimising the use of existing EU resources




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Future Perspectives: EC Communication:

- Broader Initiative: “Safe, Innovative and Accessible Medicines”
- Objectives:
 - Tackling Illegal Medicinal Products (Obj. 13-15)
 - Global Cooperation and Harmonisation (Obj. 17-22)
- Favourable environment for successful implementation & enforcement



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FOOD FOR THOUGHTS...


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Further EGA Considerations ... (1/2)

- Equal liability for all supply chain actors
 - Intermediate substance manufacturers ?
 - Involvement of transporters and logistic providers?
Pharmacists ?
- Harmonised Licensing system in the EU ?
- Harmonised import legislation ?



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Further EGA Considerations ... (2/2)

- European Inspectorate?
- New type of “Inspections” including both
 - quality aspects and,
 - financial /accounting analysis (detection of fraud)
- Joint Industry/Authorities database ?



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THANK YOU FOR YOUR ATTENTION !

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Acronyms used

- API: Active Pharmaceutical Ingredient
- MP: Medicinal Product
- GMP: Good Manufacturing Practices
- MRA: Mutual Recognition Agreement
- FDA: Food and Drug Administration (USA)
- TGA: Therapeutic Goods Administration (Australia)