# How the EXCiPACT 3rd Party Certification Scheme is helping excipient suppliers with the increasing demands for audits – the User view

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**Making Pharmaceuticals, 26th April, 2016**

**EXCiPACT asbl** is an independent, non-profit organization, established in Belgium in January 2014.

It has the following 5 Full Members

The Pharmaceutical Quality Group

As an association of associations, impartiality is assured

# Pharmaceutical Excipients
# EU Regulatory Position

**2011**

**Falsified Medicines Directive 2011/62/EU**

Qualification of excipient suppliers

**2014**

**Revision of EU GMP Part 1 Chapter 5**

Production – starting materials, 5.29 excipients

**2015**

**Guidelines on the formalized risk assessment for ascertaining** appropriate good manufacturing practice for excipients of medicinal products for human use

**- to have been implemented by 21st March 2016**

# Excipient Manufacturer's Risk Profile
# EU Regulatory Background

- **Directive 2011/62/EU , article 46 (f) :**

*'The holder of the manufacturing authorisation shall ensure that the excipients are suitable for use in medicinal products by ascertaining what the appropriate good manufacturing practice is. This shall be ascertained on the basis of a formalised risk assessment...'*

# Excipients Manufacturer's Risk Profile
# EU Regulatory Background

- **Revised EU GMP Guidelines chapter 5, section 5.27:**

*'The selection, qualification, approval and maintenance of suppliers....should be documented as part of the pharmaceutical quality system. The level of supervision should be proportionate to the risks.....The supporting evidence for each supplier / material approval should be maintained.'*

# Excipient Manufacturer's Risk Profile
# EU Regulatory Background

**2015-03-19**

**Guidelines on the formalized risk assessment for ascertaining appropriate good manufacturing practice for excipients of medicinal products for human use ……**to have been implemented by **the Manufacturing Authorisation Holder (MAH) by 21st March 2016**

- To determine the GMP required the MAH (the user) has to evaluate the risks posed
  - by the excipient in terms of the nature of the substance and then
  - by the approved suppliers who provide that substance
- These suppliers can be the Manufacturer of the excipient or a Distributor

# US Regulatory Environment

## US perspective: Excipients are Drugs

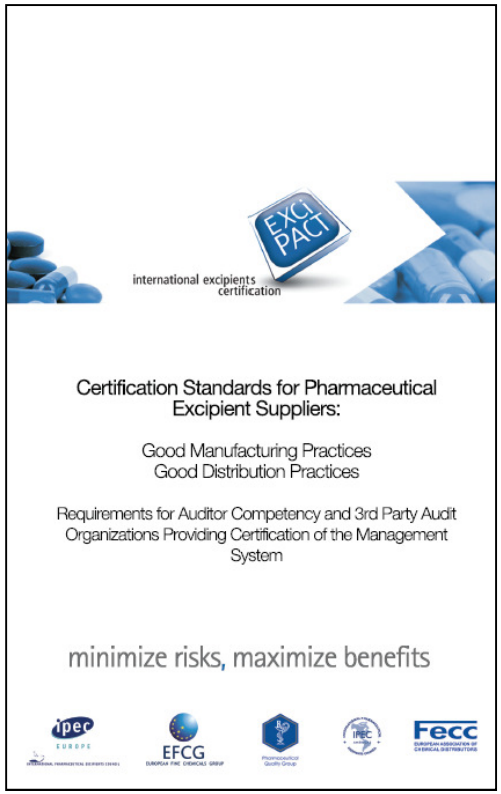
- Federal Food, Drug and Cosmetic Act Section 501(a)(2)(B) - Adulteration Provision
  - "*A drug shall be deemed adulterated -*
  - *if... the methods used in, or the facilities or controls used for, its* ***manufacture, processing, packing, or holding*** *do not conform to or are not operated or administered in conformity with* ***current good manufacturing practice*** *to assure that such drug meets the requirements of this Act as to safety and has the identity and strength, and meets the quality and purity characteristics, which it purports or is represented to possess."*
- Subject to inspection under FDA (Section 704(a)(1) of the Act) however, inspections will only be conducted by special assignment or for cause

# Issues with Physical Audits

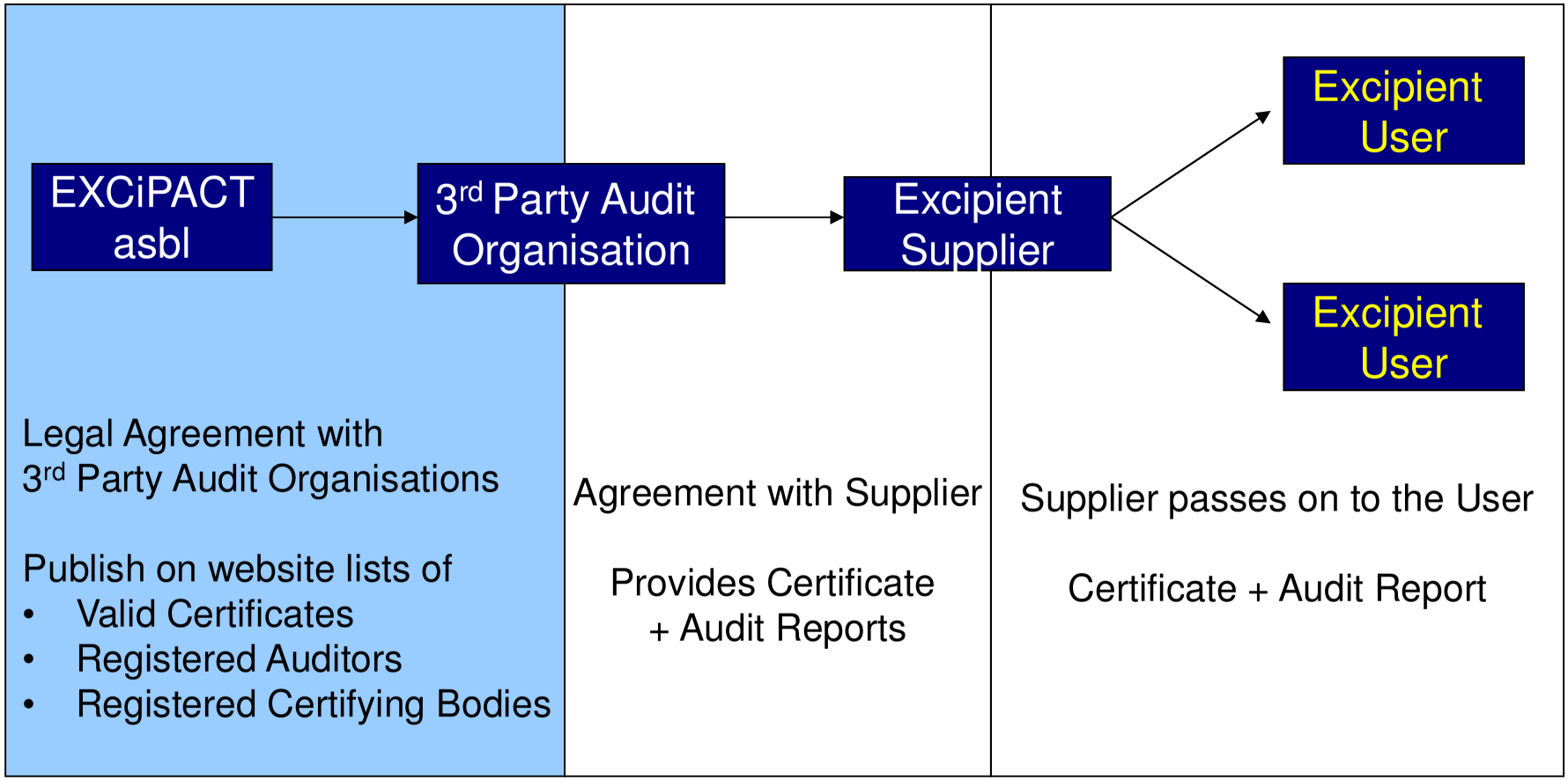
- New EU regulations  FMD 2011 → 2015
- Excipient users have to qualify their suppliers
- Expectation is they should perform a physical audit at the manufacturing site to confirm GMP is implemented
- But more and more physical audits cannot be accommodated either by suppliers or users
  - Not enough auditors or days in the year to audit all of the suppliers
  - Dilutes resources from assessing higher risks
  - Suppliers could face 100s of audit requests a year – many will be refused – what happens then?
- **An independent, high quality 3rd party audit scheme is the solution… EXCiPACT Certification**

# EXCiPACT Certification Scheme What is it?

- EXCiPACT is an independent, voluntary Certification Scheme for excipient suppliers
- Scheme was developed by suppliers and users of excipients
- Scheme Comprises the following:
  - GMP Standard for excipients
  - GDP Standard for excipients
  - Auditor Competency definition, training course, exam, and registration process
  - Certifying Body quality system definition and qualification process



# EXCiPACT Certification Scheme Process and relationship



# EXCiPACT Certification

## *Cost savings for stakeholders*

| Cost for EXCiPACT Audit | | |
|---|---|---|
| Audit fee | ~ | £9,000 |
| Certificate fee | ~ | £4,000 |
| Surveillance | ~ | £4,000 |

**Excipient Supplier**

Reduction by one two-day audit a month, plus one day for preparation, at internal cost incl. of ~ £21,000, plus ~ £4000 travel expenses per year RS1

~ £25,000 savings per year

**Pharmaceutical Company**

Reduction by one two-day audit a month , plus three days for travel and preparation of the report , ~£36,000 plus travel expenses, ~£16,000

~ £52,000 savings per year

Total cost in 3 years
~ £17,000

Total Savings in 3 years
~ £75,000

Total Savings in 3 years
~ £156,000

| Total Industry Benefit | £58,000 | £214,000 |
|---|---|---|


minimize risks, maximize benefits

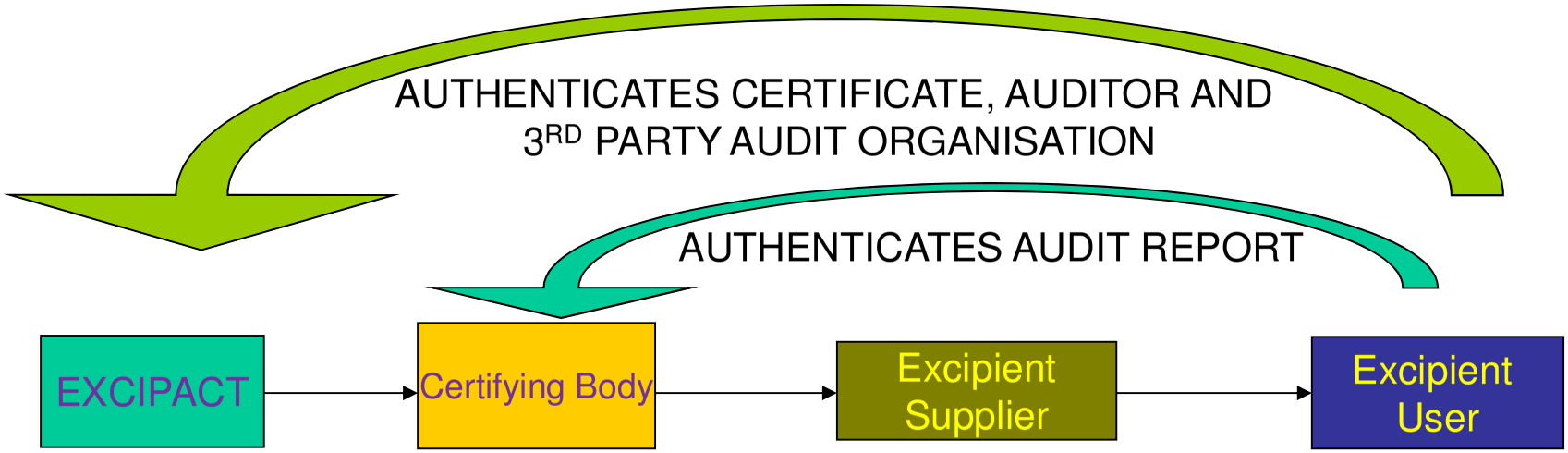
**Slide 11**

**RS1** Why travel cost for the supplier who is audited? Not clear to me. I suggest you add also the CAPA plan and actions time and resurce spend and replace the travel/

Roy, Sarbari, 17/04/2016

# Using the Certificates and Audit Reports

- Supplier issues the Certificates and Audit Reports to their Pharmaceutical Customers (Users) including any CAPA (corrective and preventive action) correspondence
- Excipient User verifies the Certifying Body, Auditor(s) and Certificate are legitimate by checking the EXCiPACT website



# EXCiPACT Certification Scheme Output

## More than a Certificate….

- Certifying Body issues Certificate + Audit Report to the supplier
- Excipient supplier makes available Certificate + Audit Reports to their pharmaceutical excipient customers/user(s)
- Scheme requires at least an annual EXCiPACT Audit so the compliance status of a supplier quickly has more depth than any 1st party audit programme
- Entire information about level of GMP/GDP of the supplier available to the pharmaceutical company for evaluation

# EXCiPACT Certification

EXCiPACT Certification Scheme will not replace ALL pharmaceutical company audits BUT…

- Significant and growing interest in the Scheme in many countries
- Both Users and Suppliers of Excipients making more and more use of the Scheme for mutual benefit without compromising regulatory compliance or patient safety
- Fully satisfies the EU Guidelines on ascertaining GMP/GDP for excipients
- Helps reduce costs for both suppliers and users by reducing the audit burden

# Supplier-initiated process
# A concern for Users?

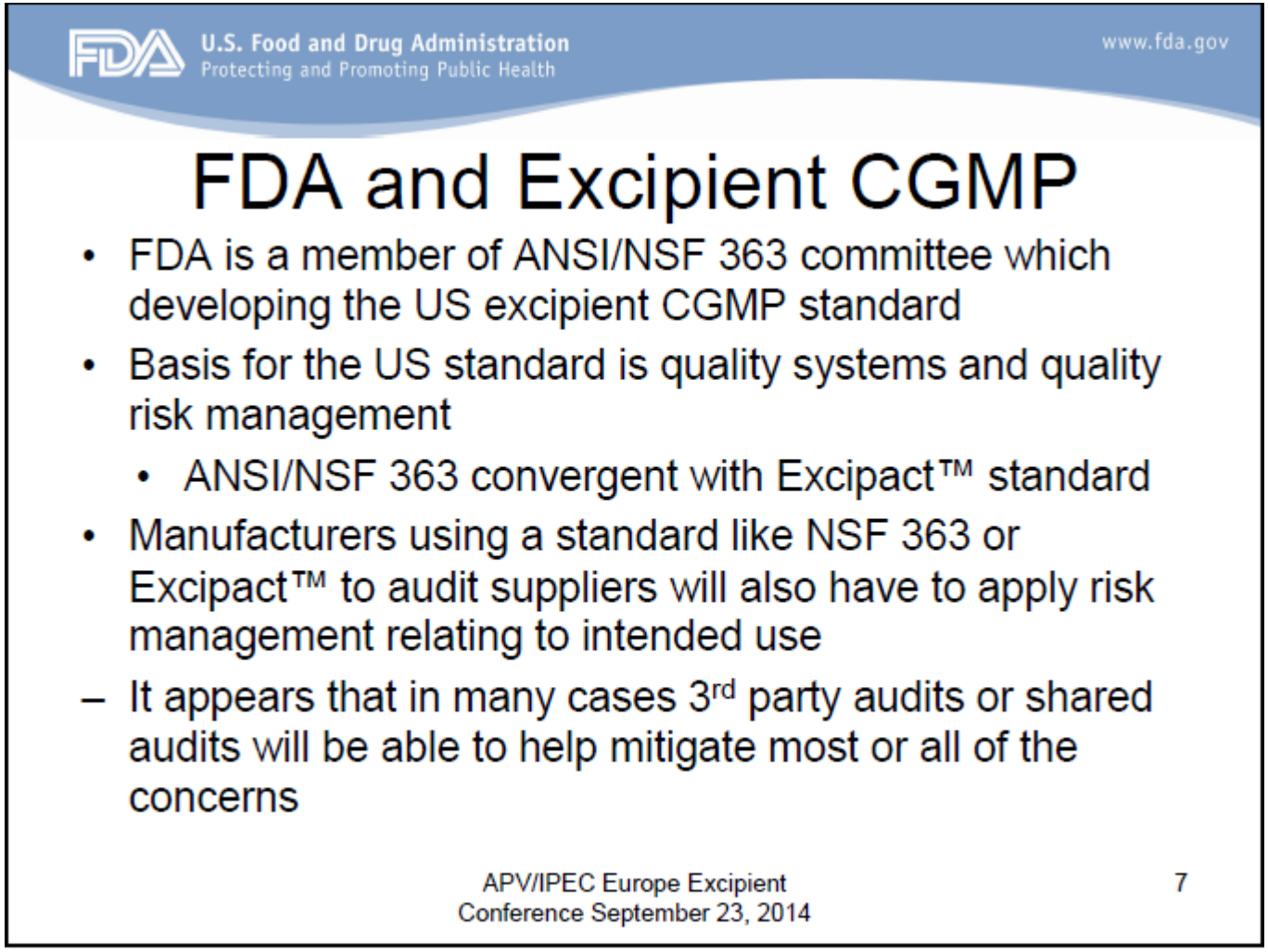
- As the Supplier contracts with the Certifying Body there could be a concern that the Supplier will have undue influence over the audit process
- Yes, it is a hazard – BUT the oversight applied by EXCiPACT asbl mitigates the risks by independent auditor registration and reregistration, witnessed audits and regular audits of the Certifying Body

# EXCiPACT
# What do Authorities say?

- At the European EXCiPACT launch in Barcelona, January 25, 2012, Richard Andrews from the UK's **MHRA** stated:
  - "3rd Party certification schemes can assist medicinal product manufacturers in achieving compliance with GMP at reduced cost and impact on time and resource".
  - "Such schemes will also benefit excipient manufacturers as they should reduce the number of audits they are required to host with the consequential reduction in time and cost".
  - "Overall patient safety should be enhanced"

# EXCiPACT
# What do Authorities say?

- Dr Steven Wolfgang
- APV Excipient Conference Dusseldorf Sept 23rd 2014



# EXCiPACT Certification Scheme
# What Users say?

- "We are obtaining and evaluating any existing 3rd party certification audit reports during the excipient supplier audit planning and preparation process – these are fed into the supplier audit risk assessment process". Inference: suppliers with EXCiPACT Certificates are lower risk…
- "The EXCiPACT Certificate and Audit Report allowed us to increase audit frequency and spend half a day on site rather than a full audit"
- "Helps avoid *duplication of effort* …..since each element of the excipient GMP standard is already periodically assessed"
- "If an audit is deemed necessary, its scope could then be focused on specific topics that are not already addressed by the certification standard"
- "EXCiPACT audit reports provide an expedient and cost effective means for excipient users to assess GMP/GDP conformance of suppliers, which is needed to demonstrate ongoing supplier qualification".

# User View - Summary

- EXCiPACT audits cover most low-medium risk situations
- Permits user's own auditors to focus on higher risk situations
- EXCiPACT audit cost savings are attractive
- Opportunity for savings to increase as EXCiPACT audits/year increase
- 30 certificates for international sites to date with 4 more in progress

**Conclusion**

**As suppliers continue to achieve EXCiPACT certification, its benefits to the pharmaceutical industry to reduce the audit burden will continue to be even more fully realised.**

# EXCiPACT – Users' View
# Reducing the Audit Burden

**for further information visit**

**www.excipact.org**

## Thank You for your attention!

# EXCiPACT
# Registered Certification Bodies

- 2012: Launched in Europe - 2 Registered Certifying Bodies
- 2013: First Certificates issued
- 2016: 6 Registered Certifying Bodies
- 2016: 30 Certificates issued to date

*For details of Registered Certifying Bodies and Registered Auditors see [www.excipact.org](http://www.excipact.org)*


**minimize risks, maximize benefits**

# 2016 Certificates' Status Report

30 Certificates Issued

| | |
|---|---|
| • Belgium (2) | Capsugel, Lanolines Stella |
| • Canada (1) | A&C American Chemicals |
| • China (1) | Boai NKY |
| • France (5) | Croda, Capsugel, Novacarb, Roquette, Sepiprod, |
| • Germany (9) | Aug. Hedinger, BASF, Biogrund, Budenheim, Evonik, Grace, Merck, Meggle |
| • India (4) | Ideal Cures (3), Vikram Thermo |
| • Netherlands (1) | Sonneborn |
| • Saudi Arabia (1) | Saudi Kayan |
| • Singapore (1) | Croda |
| • Spain (1) | Croda |
| • UK (3) | Colorcon, Croda (2) |
| • USA (2) | Ashland (2) |

1

*For full details of Certificate holders – see [www.excipact.org](http://www.excipact.org)*

# Latest EU Guidelines

- Excipient suppliers that hold an EXCiPACT GMP and to GDP Certificate are a major asset to the excipient users
- Sharing the audit reports on a continual basis will ensure that not only are the needs of the initial risk assessment satisfied but also the continuing evaluation as well
  - A win for the supplier
  - A win for the user
  - A win for the regulator
  - A win for the patient