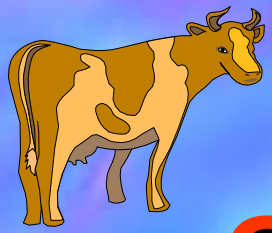
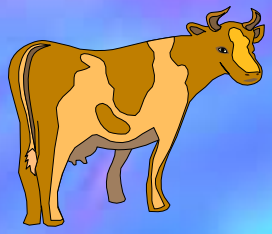


Commission Directive

2003/32/EC

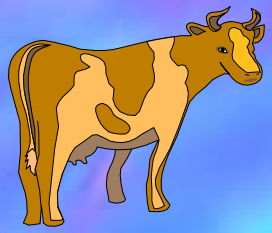
THIERRY CHIGNON

Quintiles Consulting Europe



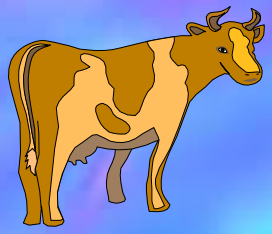
WHY?

- **(1)** "On 5 March 2001 **France** adopted a **national** measure **prohibiting** the manufacture, placing on the market, distribution, import, export and use of *dura mater* substitutes manufactured from materials of animal origin.
- (2) France justified the measure by the uncertainties that exist with regard to the **risk of transmission to humans of animal spongiform encephalopathies** from such medical devices, and by the fact that **alternatives are available**, in the form of synthetic materials or autologous materials.



WHY?

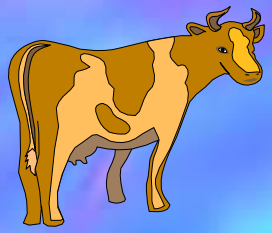
- ⇨ **COMPARISON**
- **OF YOUR DEVICE TO**
- **SUITABLE ALTERNATIVES!**



WHY?

- (6) In order to **improve the level of safety and health protection**, it is necessary to further **reinforce** the protective measures against the overall risk of transmitting animal spongiform encephalopathies via medical devices.

⇨ **Precautionary Principle**

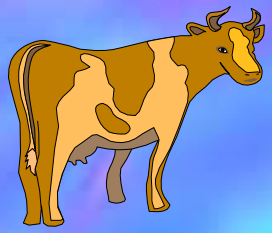


WHY?

- ⇨ **CE Mark**

  IS NOT

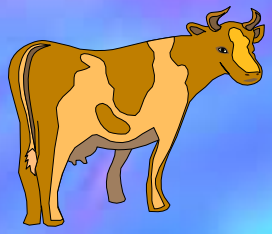
  SUFFICIENT...



SCOPE

- Commission Directive 2003/32/EC of 23 April 2003 introducing detailed specifications as regards the requirements laid down in Council Directive 93/42/EEC with respect to MD manufactured **utilizing** tissues of animal origin".

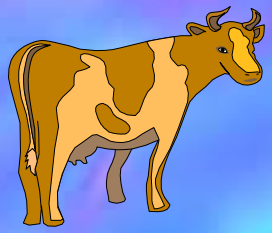
⇨ **"utilizing" not "containing"**



SCOPE

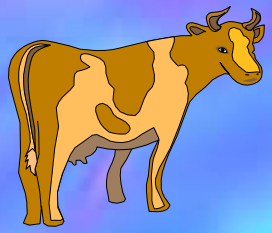
- ⇨ **France raised an issue while transposing since 2003/32/EC mentions "utilizing" everywhere except in article 5 section 4:**

"...the risk analysis and risk management of the tissues or the derivatives intended to be <u>incorporated</u> in the medical device as established by the manufacturer"



SCOPE

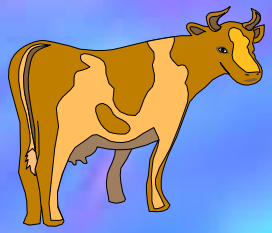
- The animal tissues covered by this Directive are those originating from **bovine, ovine and caprine** species, as well as deer, elk, mink and cats.



SCOPE

- ⇨ **Naturally**

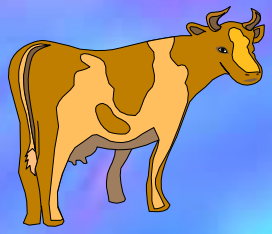
  TSE affected Species



SCOPE

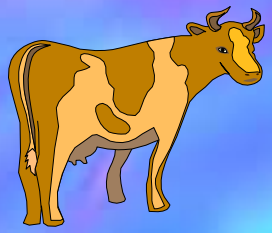
- This Directive **does not apply** to medical devices referred to in the first paragraph, which are **not intended to come into contact** with the human body or which are intended to **come into contact with intact skin only**.

⇨ **Just class III medical devices**



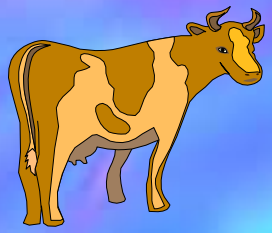
SCOPE

- ⇨ MD just utilizing tallow derivatives are not in the scope of this Commission Directive although the Risk Management dossier shall take into account the relevant requirements established in this Directive



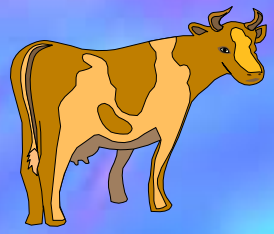
NOTIFIED BODY

- MSs shall verify that Notified Bodies **have up-to-date knowledge** in order to assess...
- If it is necessary for a MS to amend the tasks of a notified body, that MS shall notify the Commission and the other MSs accordingly.



NOTIFIED BODY

- ⇨ Confirmation of NB notification: still pending...



NOTIFIED BODY

Notified bodies shall evaluate the manufacturer's risk analysis and risk management strategy, and in particular:

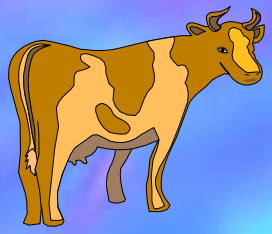
(a) the information provided by the manufacturer

(b) the justification for the use of animal tissues or derivatives

(c) the results of elimination and/or inactivation studies or of literature search

(d) the manufacturer's control of the sources of raw materials, finished products and subcontractors

(e) the need to audit matters related to sourcing, including third party supplies.

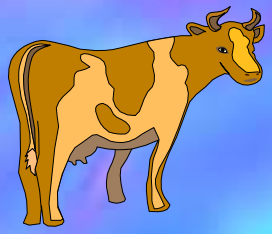


JUSTIFICATION

Justification for the use of animal tissues or derivatives.

- The manufacturer **must justify**, on the basis of his overall risk analysis and risk management strategy, the decision to **use animal tissues or derivatives**, (specifying animal species and tissues) taking into account the expected clinical benefit, potential residual risk ...
- … and **suitable alternatives**.

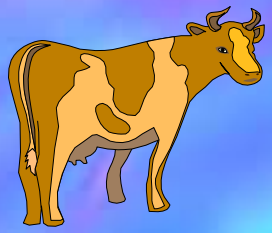
⇨ **regardless the procedure followed**



EDQM TSE CERTIFICATE OF SUITABILITY

Notified bodies shall, during the evaluation of the risk analysis and risk management, take account of the **TSE certificate of suitability** issued by the European Directorate for the Quality of Medicines, for starting materials, where available.

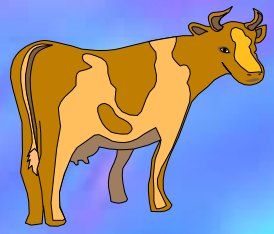
⇨ **First interest of TSE CoS**



EDQM TSE CERTIFICATE OF SUITABILITY

Except for medical devices using starting materials for which a TSE CoS has been issued, national bodies shall, through their competent authority, seek the opinion of the competent authorities of the other Member States on their evaluation of and conclusions...

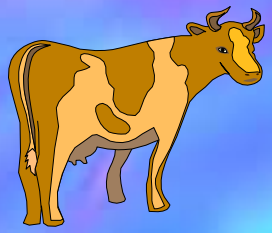
⇨ **Second interest of TSE CoS**



COMPETENT AUTHORITY ASSESSMENT

- NB shall, through their competent authority, seek the opinion of the competent authorities of the other Member States …
- Before issuing an EC certificate, the NB shall give due consideration to any comments received within 12 weeks from the date on which the opinion of the national competent authorities was sought.

⇨ **Opportunity for all MSs to comment…**



1 - Justify animal origin

2 - Compare to suitable alternatives

3 - Demonstrate TSE safety

EDQM TSE CoS?

YES

NO

NB assessment of 1 & 2

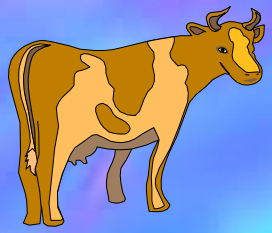
NB assessment of 1, 2 & 3

TSE CE Certificate

CA assessment

Other CAs assessments

TSE CE Certificate



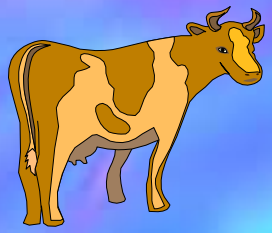
TRANSPOSITION

- Member States shall adopt and publish **before 1 January 2004** the provisions necessary to comply with this Directive.

  …

- They shall apply those provisions with **effect from 1 April 2004.**

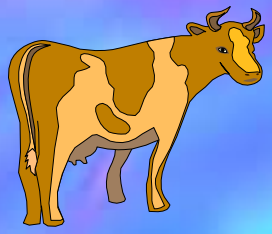
⇨ **Delay?**



IMPLEMENTATION

- Until 30 September 2004, Member States shall accept the placing on the market and the putting into service of MD which are covered by an EC certificate issued before 1 April 2004.

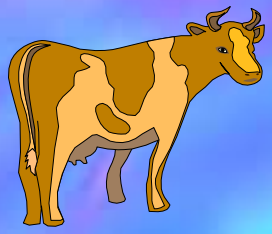
⇨ 30 September 2004…



IMPLEMENTATION

- ⇨ **Flexibility to be considered:**

Same date but OK for dossiers having been filed BUT still under assessment



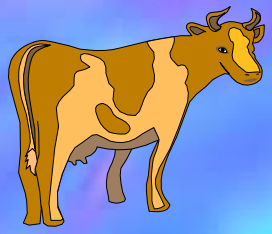
TSE SAFETY STEPS

- There are two key steps that must be considered:

— **selecting starting materials** (tissues or derivatives) considered appropriate regarding their potential contamination with transmissible agents taking into account further processing,

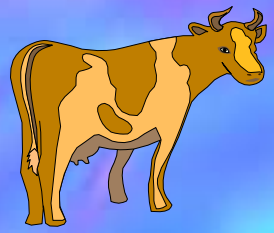
— **applying a production process to remove or inactivate transmissible agents** on controlled sourced tissues or derivatives.

⇨ **EN12442 parts 2 and 3**



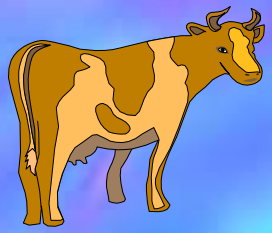
SCIENTIFIC OPINIONS

- In performing the risk analysis and risk management strategy, due consideration must be given to opinions adopted by the relevant scientific committees [SSC], and where appropriate to the opinions of the CPMP



TSE SAFETY

- Animals as a source of material (younger = safer)
- Geographical sourcing (GBR level)
- Nature of starting tissue (new infectivity tables/cross-contamination)
- Inactivation/removal of TSE agents (study or literature)
- Quantities of animal starting tissues or derivatives required to produce one unit of the medical device
- Tissues or derivatives of animal origin coming into contact with the patients and users
- Route of administration



DIRECTIVE 2003/32/EC

Thank your for your attention

Questions?