I dossier di AIC: stato dell'arte

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AIFA

Dichiarazione di trasparenza/interessi*

Le opinioni espresse in questa presentazione sono personali e non impegnano in alcun modo l'AIFA

Interessi nell'industria farmaceutica	NO	Attualmente	Da 0 a 3 anni precedenti	oltre 3 anni precedenti
INTERESSI DIRETTI:				
1.1 Impiego per una società: Ruolo esecutivo in una società farmaceutica	X	☐	☐	☐ obbligatorio
1.2 Impiego per una società: Ruolo guida nello sviluppo di un prodotto farmaceutico	X	☐	☐	☐ obbligatorio
1.3 Impiego per una società: altre attività	X	☐	☐	☐ facoltativo
2. Consulenza per una società	X	☐	☐	☐ facoltativo
3. Consulente strategico per una società	X	☐	☐	☐ facoltativo
4. Interessi finanziari	X	☐	☐	☐ facoltativo
5. Titolarità di un brevetto	X	☐	☐	☐ facoltativo
INTERESSI INDIRETTI:				
6. Sperimentatore principale	X	☐	☐	☐ facoltativo
7. Sperimentatore	X	☐	☐	☐ facoltativo
8. Sovvenzioni o altri fondi finanziari	X	☐	☐	☐ facoltativo
9. Interessi Familiari	X	☐	☐	☐ facoltativo

* Lorenzo Montrasio, secondo il regolamento sul Conflitto di Interessi approvato dal CdA AIFA in data 25.03.2015 e pubblicato sulla Gazzetta Ufficiale del 15.05.2015 in accordo con la policy EMA /626261/2014 sulla gestione del conflitto di interessi dei membri dei Comitati Scientifici e degli esperti.

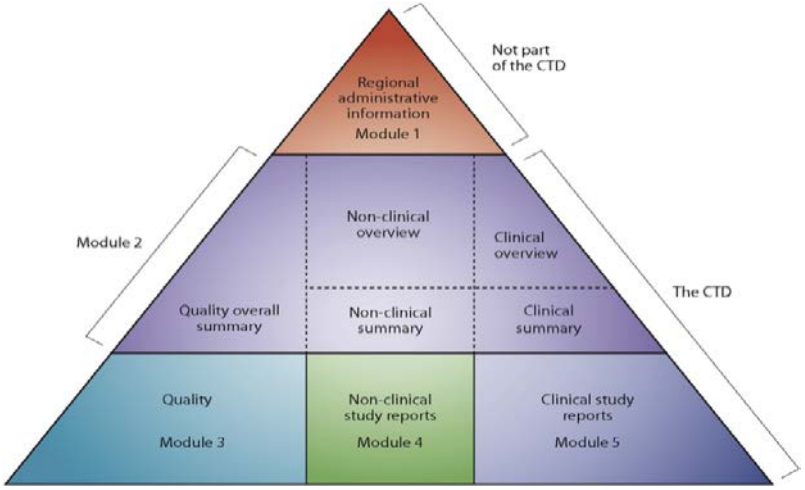
N.B. Per questo intervento non ricevo alcun compenso

Dossier di AIC

- EU Directives e Regulations
- European Pharmacopeia
- Guidelines
- CTD ICH

Dossier di AIC

- Volume 2B
- Notice to Applicants
- Medicinal products for human use
- Presentation and format of the dossier
- Common Technical Document (CTD)



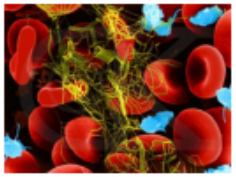
https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-2/b/update_200805/ctd_05-2008_en.pdf

Types of Biological Products

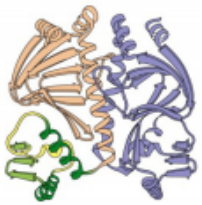
Blood Derivatives

Whole Blood

Blood Components

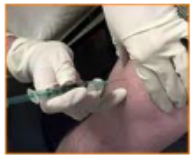


Proteins

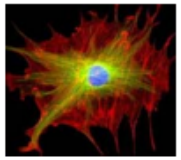


Human Tissues

Vaccines (preventive *and* therapeutic)



Allergenic Extracts



Cellular & Gene Therapies

Xenotransplantation Products

Module 1

Administrative information and Prescribing information

1.0 Cover Letter

1.1 Comprehensive table of content ---

1.2 Application Form Administrative Data

1.3 Product Information Summary of Product Characteristics, Labelling and Package Leaflet

1.4 Information about the Experts Expert Reports: Signature of Experts

1.5 Specific Requirements for different types of applications ---

1.6 Environmental risk assessment Environmental risk assessment

1.7 Information relating to Orphan Market Exclusivity

1.8 Information relating to Pharmacovigilance

1.9 Information relating to Clinical Trials

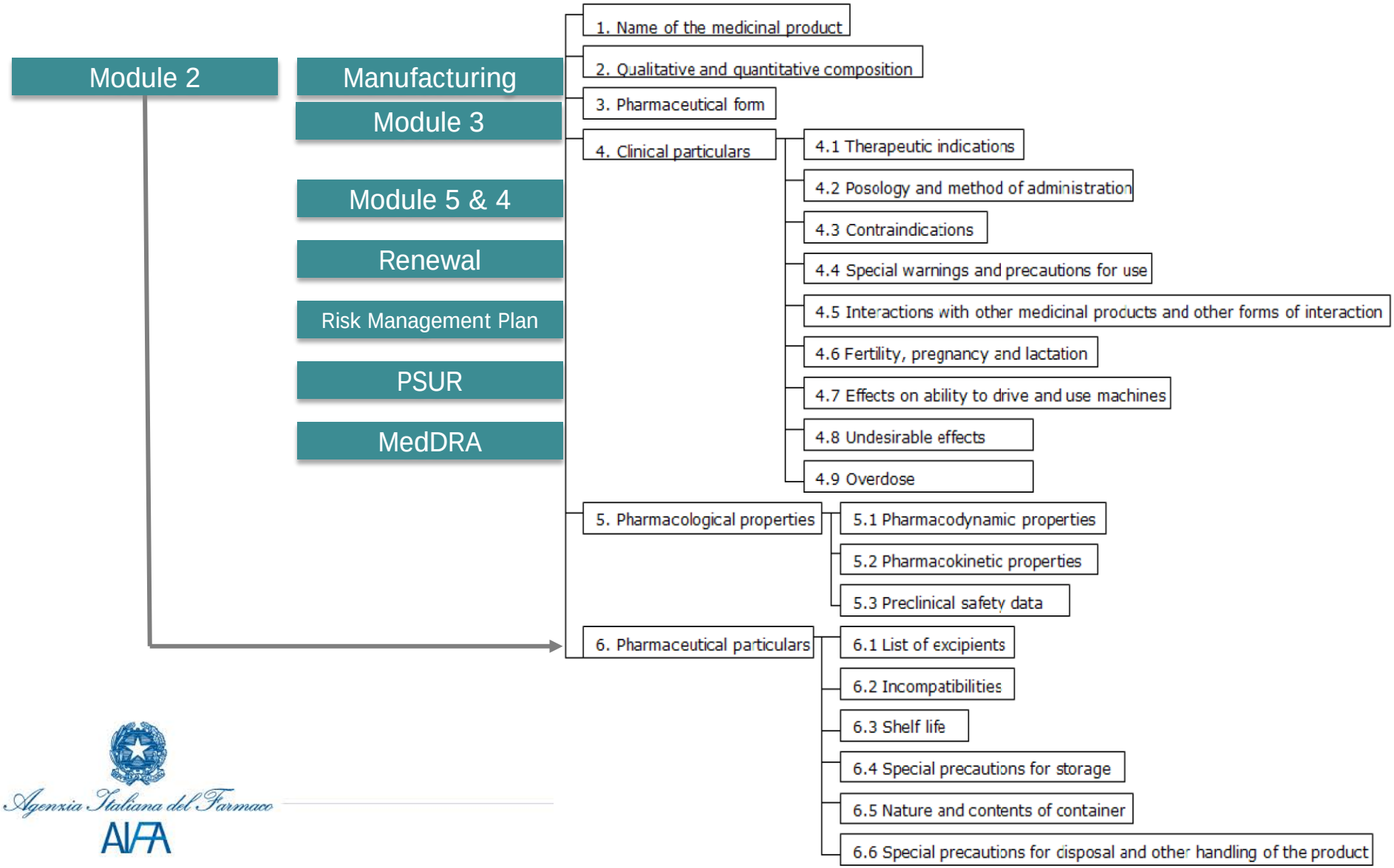
1.3 Product Information Summary of Product Characteristics, Labelling and Package Leaflet

Product Information Summary

Package Leaflet

Readability test

Summary of Product Characteristics



Products for immunotherapy and *in vivo* diagnosis

Regulatory strategy

Scientific criteria

Extrapolation

Flexibility

1. MA presentation
2. Homologous groups
3. Allergen Mixtures
4. Changes in the manufacturing process

Manufacturing & Quality: Drug Substance

Source material

Raw material

Starting material

Active Substance

- Traceability
- Adventitious Agents
- In process control/limits

- ❑ Appearance & description
- ❑ Identity, purity and impurities,
- ❑ Total allergenic activity and major allergen determination
- ❑ Potency assays

Nota AIFA 2010: Modulo 3.2.S

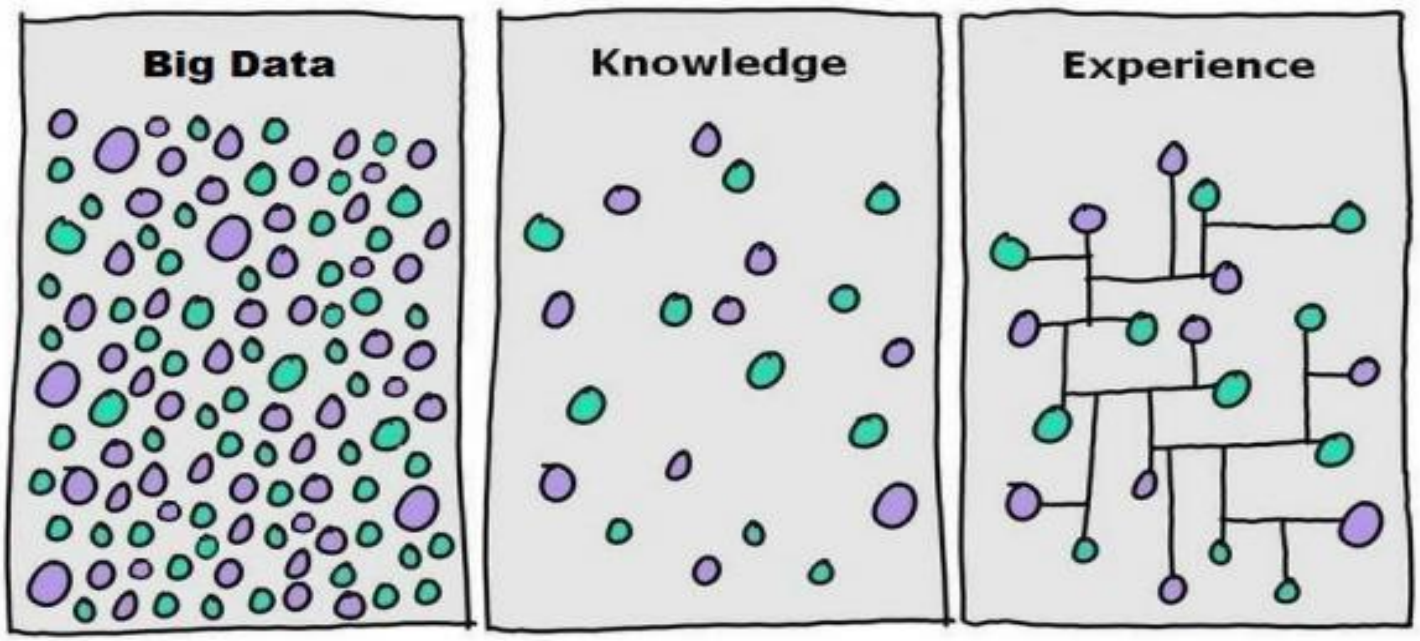
Allergeni preparati secondo modalità seriali e standardizzate tipiche di un processo industriale.

10 Aziende
283 Dossier mod. 3.2.S

Major concerns:

- Documentation
- Charactherization
- Manufacturing process validation
- Analitical method validation
- Lack of stability data

Dossier AIC: Documentation



R&D AIC

Manufacturing & Quality: Drug Pruduct

- Sterility
- Microbial contamination
- Protein content
- Protein profile
- Allergen profile
- Total allergenic activity
- Individual allergens

In House Reference Preparation

Verification of batch to batch consistency

Characterization:
- Protein content and profile
- Relevant allergens
- Individual allergens

Biological potency:
- *in vivo* technics
- *in vitro* methods

Pooled sera from allergergic patients

Safety & Efficacy

Module 2
Overview & Summary

Module 4
Nonclinical Study Reports
Pharmacology
Pharmacokinetics
Toxicology
Literature references

Module 5
Clinical Study Reports

Guideline on the clinical development of products for specific immunotherapy for the treatment of allergic diseases

Conclusions

The CTD is an internationally agreed format for the preparation of applications to be submitted to regulatory authorities in the three ICH regions of Europe, USA and Japan. It is intended to save time and resources and to facilitate regulatory review and communication.

The CTD gives no information about the content of a dossier and does not indicate which studies and data are required for a successful approval

Conclusions

Provide accepted norms and standards for the evaluation

To help applicants obtaining marketing authorisation

To guarantee a harmonised approach of assessment and to support the decision process

Written standards (i.e. legislation and guidelines)
Laboratory standard (i.e. Harmonised Methods; I.S.)

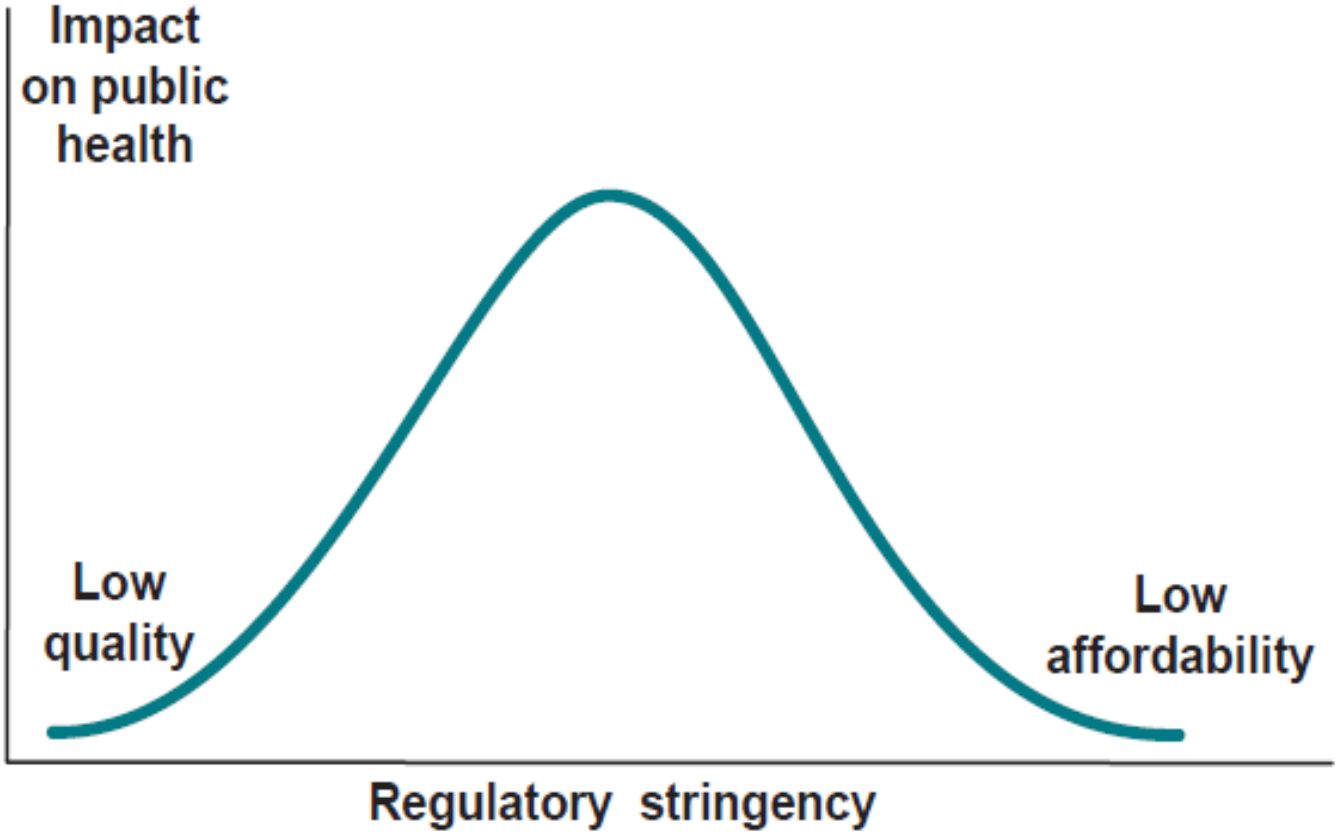
Conclusions

- Documentation of all relevant parameters for the allergens within a given extract is complex due to the high number of allergens in an allergen extract and the cross-reactivity of the individual components.

- Mechanism of action regarding the clinical effect of specific immunotherapy is up to now not fully understood

- There is a wide variety of study designs in terms of dosages, study duration, inclusion criteria, end-points chosen, analysis of data, and control of environmental variables in the evaluation of products for immunotherapy

Conclusions



CONTATTI

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