



Regulation of Allergen Products - State of the Art and New Developments: Current and future activities in national regulation of allergen products (including named patient products (NPP))

Update from Italy

Milica Mitrevski

03/09/2026



# Public Declaration of transparency/interests\*

The view and opinions expressed are those of the individual presenter and should not be attributed to AIFA

| Interests in pharmaceutical industry                                                    | NO                                  | Current                  | From 0 to 3 previous years | Over 3 previous years              |
|-----------------------------------------------------------------------------------------|-------------------------------------|--------------------------|----------------------------|------------------------------------|
| <i>DIRECT INTERESTS:</i>                                                                |                                     |                          |                            |                                    |
| 1.1 Employment with a company: pharmaceutical company in an executive role              | <input checked="" type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/>   | <input type="checkbox"/> mandatory |
| 1.2 Employment with a company: in a lead role in the development of a medicinal product | <input checked="" type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/>   | <input type="checkbox"/> mandatory |
| 1.3 Employment with a company: other activities                                         | <input checked="" type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/>   | <input type="checkbox"/> optional  |
| 2. Consultancy for a company                                                            | <input checked="" type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/>   | <input type="checkbox"/> optional  |
| 3. Strategic advisory role for a company                                                | <input checked="" type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/>   | <input type="checkbox"/> optional  |
| 4. Financial interests                                                                  | <input checked="" type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/>   | <input type="checkbox"/> optional  |
| 5. Ownership of a patent                                                                | <input checked="" type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/>   | <input type="checkbox"/> optional  |
| <i>INDIRECT INTERESTS:</i>                                                              |                                     |                          |                            |                                    |
| 6. Principal investigator                                                               | <input checked="" type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/>   | <input type="checkbox"/> optional  |
| 7. Investigator                                                                         | <input checked="" type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/>   | <input type="checkbox"/> optional  |
| 8. Grant or other funding                                                               | <input checked="" type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/>   | <input type="checkbox"/> optional  |
| 9. Family members interests                                                             | <input checked="" type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/>   | <input type="checkbox"/> optional  |
| 10. Serious reasons of convenience                                                      | <input checked="" type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/>   | <input type="checkbox"/> optional  |

\***Milica Mitrevski**, in accordance with the Regulation for the prevention and handling of conflicts of interest of the Italian Medicines Agency, approved by AIFA Board of Directors (Resolution no. 9 - 12 February 2025).

N.B. I am not receiving any compensation

## Disclaimer

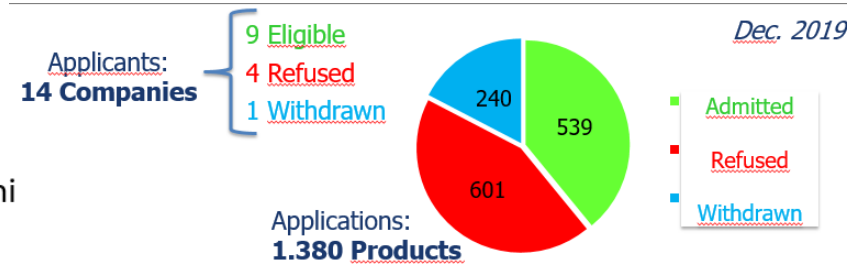
The views expressed in this presentation are the personal views of the presenter and may not be understood or quoted as being made on behalf of or reflecting the position of the respective national competent authorities, the European Medicines Agency, or one of its committees or working parties.

- ☐ Allergen products in Italy since 1991: regulatory background
- ☐ Regulation of allergens marketed «*ope legis*» (by operation of law), NPP
- ☐ **Update on regulation of haptens in Italy and other activities regarding allergens**
  - ☐ Temporary authorisation of clinical use of indispensable haptens
  - ☐ AIFA Technical Committee and National Guide document
  - ☐ Reduction of fees for allergen products
  - ☐ AIFA participation in EU allergen working groups
  - ☐ MA application status of haptens in Italy
  - ☐ Current regulatory status and critical issues
  - ☐ Analysis of applicability of Zero Day MRP procedure
  - ☐ Italian Pharmacopoeia – work on a new general chapter
- ☐ **Conclusions and way forward**

- Allergen products considered as medicines in EU already for several decades (Dir. 89/342/CEE)
- In 1991, the Italian Ministry of Health allowed allergen products already available on the market to remain marketed, provided that a MAA was submitted and the applicable fees were paid
- Aim: to avoid sudden shortages and permit temporary stay on the market with authorization «*ope legis*», pending MA
- Over the years, several other allergen products were placed on the Italian market (many as NPP)
- Only a few allergen products had regular DCP/MRP authorisations
- Different AIFA recognition activities of allergen products over the years, still inconclusive

- AIFA issued **Res. 2130/2017**, to restart the registration process of allergens marketed «*ope legis*»
- 1° step: evaluation of **eligibility** of the resubmitted MAA (by the end of 2019)
- 2° step (ongoing): evaluation of **resubmitted e-CTDs**
- Updated lists of «*ope legis*» allergens (Admitted/Refused/Withdrawn)

<https://www.aifa.gov.it/en/web/guest/medicinali-allergeni>



*Refused/Withdrawn products could be no more marketed (with some exemptions)*

- Dossiers of **AITs** marketed «*ope legis*»:
  - supportive evidence of heterogeneous level and **overall** insufficient (preliminary assessment)
  - classification based on the clinical data provided in the dossier to adopt an adequate regulatory strategy
  - therapeutic continuity guaranteed

- Large number of allergen products has been marketed in Italy pursuant to art. 5 of Leg. Decree 219/2006, as **"Named Patient Product" (NPP)**, or "*... industrially prepared medicines at the request, written and unsolicited, of the doctor, [...] who undertakes to use the aforementioned medicines for a specific patient or for a patient staying in the facility where s/he works, under his/her direct and personal responsibility ...*"
- Discussion at national level (**Leg. Decree 219/2006**) on the legal basis **"magistral formula (art.3)"** and **"NPPs (art.5)"** as these are legally bound to art.5 of Law 94/1998 "Di Bella Law") for medical prescription (Active substance in monographs of national/EU Pharmacopeia or with MA in EU)

# **Update on regulation of haptens in Italy** and other activities regarding allergens

- Rejection/withdrawal of various **haptens** in the 1° step + withdrawal of patch tests marketed as devices or NPP □ **unmet clinical need**
- In collaboration with pharma companies and the scientific society SIDeMaST □ a **published list of currently used indispensable haptens** for patch tests
- AIFA issued **Res. 1334/2021** (as amended) for **temporary authorisation of clinical use** of GMP-produced haptens without MA and not available «*ope legis*», transitionally (24 months), pending their regulation. The annex provides the complete list of all haptens available on the market through the Resolution, ope legis and MAs, comprising approximately 370 products
- **Res. 442/2023:** renewed the temporary authorisation for a further 36 months; after expiry (**by the end 2026**), these products can no longer be marketed unless the company submits a MAA before the deadline

**Interdisciplinary Technical Committee** on the clinical use of haptens set up in AIFA in March 2022 (monthly meetings) to better address regulatory solutions

Clinicians from scientific societies and regulatory experts and assessors from AIFA

**National guide document** elaborated, including **revised national SIDAPA series, baseline (adult/pediatric) and supplementary**, with haptens at optimal formulation (following rigorous revision of available published data)

Aimed to favour the efficacious regulation and authorization of haptens necessary for the clinical practice

[https://www.aifa.gov.it/documents/20142/1812950/Regolamentazione\\_uso\\_clinico\\_apteni\\_patch\\_test\\_rev.1.pdf](https://www.aifa.gov.it/documents/20142/1812950/Regolamentazione_uso_clinico_apteni_patch_test_rev.1.pdf)

Regolamentazione  
e uso clinico  
degli apteni per  
*patch test*

- Since 2023 Italy introduced a **reduction of fees for all allergen products** (therapeutic / diagnostic) for national/MRP/DCP MAA/Renewal/variations
- Regarding allergen medicinal products, Article 3 of the Decree of the Minister of Health dated 13 September 2023, states that "*the annual fee payable to AIFA by each Marketing Authorisation Holder shall be **one-third** of the fee specified in Article 4(5) of Decree of the Minister of Health No 53 of 29 March 2012*"
- For MAA of diagnostic allergen products the fees are reduced down to **tenth** of the regular fees; for MAA of therapeutic allergen products applicable fees were reduced to **one quarter** of the regular fees

- **CMDh Allergen group:**

- continuous active participation of Italy over the years, with more recent focus on haptens
- to achieve a common approach across the EU and good collaboration and exchange of opinions among the MS

- Active contribution on **drafting of the EMA guideline** "*Allergen products development for immunotherapy and allergy diagnosis in moderate to low-sized study populations*" (EMA/161669/2025)

First harmonised EU framework to provide general guidance on the development of medicinal products for the diagnosis and immunotherapy of allergies, if only moderate to low-sized study populations are available

- **9 haptens for patch test result approved** (for one of them IT acted as a RMS in a MRP procedure)
- Other **ongoing** procedures, national and MRP, of haptens in Italy
- Some of them, **under evaluation**, are haptens not marketed "*ope legis*" but **currently in use** in Italy with temporary authorisation (**Res. 1334/2021** (as amended)) within the baseline series

- The Agency contacted SmartPractice (SPE) and Chemotechnique (CT) after the AIFA Director General's Decision 442/2023 that will be expired at year-end
- SPE decided to submit MAA for national baseline series for adults and paediatric patients (2026-2028), some dossiers already submitted and under evaluation
- CT would be interested in EU baseline series, without any concrete regulatory action up to now
- Despite reduction of fees in Italy, very limited number of MAA at the moment

**Therefore, only a very limited number of haptens will obtain a MA,  
insufficient to satisfy the clinical need**

## Further steps taken/ongoing

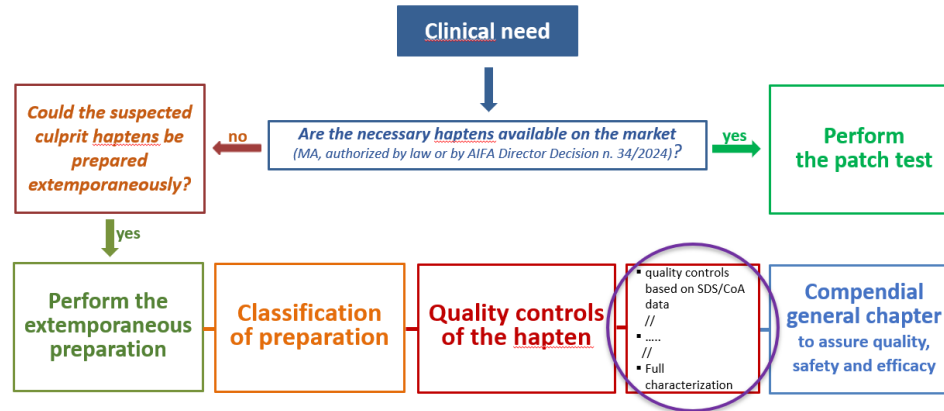
1. Analysis of applicability of Zero Day MRP procedure
2. General Chapter of Italian Pharmacopea for extemporaneous preparations of haptens not available on the market

- Zero Day MRP procedure for the epicutaneous patch tests: "administrative" MRP, shortened timetable, no comments from CMS on quality and clinical modules; only common version of the currently approved PIs
- Acceptable on exceptional basis, products currently or potentially at risk of shortage in Italy (CMDh/451/2024)
- Analysis of regulatory and manufacturing status, sales volumes for haptens included in supplementary series from Det. 442/2023 (expire by the end of 2026) with MA in Germany (but no *ope legis* – not affected by expiry )
- Many potentially eligible product dossiers are old and unclear if recently updated

**18 haptens identified as potentially eligible; however with (very) low sale volumes in Italy and no interest of Company for MA in Italy**

**Currently not a viable solution in the specific context of Italian market**

- Work ongoing on a general chapter in Italian Pharmacopoeia for extemporaneous preparations of haptens not available on the market
- To ensure the availability of **rare or emerging haptens** not otherwise accessible on the market (ex art. 3, Dir. 2001/83).



### Main critical issues:

- identifying analytical methods that most hospital pharmacies can readily perform
- hospital pharmacies not currently equipped to assume this additional workload in terms of costs, organization, staffing, time and specialized expertise

- Relatively high number of haptens without MA in EU, not eligible for MRP
- Low interest of companies in MRP other than haptens of baseline series
- Limited number of haptens not currently manufactured

**Further solutions needed at national level for haptens and overall for allergen products**

**Further dialogue and exchange of views and possible common solutions among MS would be valuable**

**Continuous efforts in EU to regulate allergen medicinal products**

**All stakeholders could benefit from harmonised approaches in EU**

## Allergies - a **growing public health concern**

Regulatory efforts, both on national and EU level - necessary to **improve access of allergen products** with ensured **quality, efficacy and safety**



Thank you for your attention!  
[m.mitrevski@aifa.gov.it](mailto:m.mitrevski@aifa.gov.it)

[aifa.gov.it](http://aifa.gov.it)

