

**Agence fédérale des médicaments
et des produits de santé**

**Federal agency for medicines & healthcare
products**

**National Scientific & Technical/Regulatory
Advice: current procedures & experience**

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DG PRE Authorisation

Outline of Presentation

- main STA-KM unit activities
- current evolutions
- future initiatives & challenges



7 years national STA unit @ FAMHP: where do we stand ?



- Official start: april 2009
- STA unit: 4,8 FTE
- Mission: stimulate R&D, innovation and early access to new innovative medicines to the patients' benefit
- Focus: early dialogue & stakeholder engagement
- How: providing multidisciplinary scientific-regulatory guidance & expertise throughout the product lifecycle!



1. Core activities: STA unit

1. Coordination of scientific advice requests

- Treatment & consistent follow-up of **national scientific-technical (STA) advice requests** (BE, other NCA's,)
- Consistent follow-up of **European advices (EMA - SAWP)**
in relation to CTA's, PIP's, MAA's, biomarker qual., PA, joint SAWP-HTA, development programs,...
- Consistent follow-up of **European decisions & guidelines** (CHMP, PRAC, COMP, CAT,, EC)
- Assuring **quality & harmonisation of opinions**
- Interface with ≠ FAMHP depts. & directorates

2. Admin. support & proactive interaction with BE SAWP (H/V) members



1. Core activities: STA unit

3. Networks of external experts

famhp D-base: > 700 experts (of which > 600 external)

4. Active “horizon scanning”: R&D developments, regulatory evolutions, rare diseases & unmet medical needs, early access mechanisms, ...

5. Coordination of:

- Portefolio meetings:

eg. company presentation, overview of R&D pipeline, therapeutic areas,...

- Info meetings

eg. R&D projects, biomarkers, biosimilars, ...

= early dialogue tools prior to formal STA procedures !



2: National STA: procedure updates

- voluntary procedure
- specific questions
- expert responses are prepared & discussed internally
- outcome :
 - written advice (Type I)
 - scientific advice meeting & written advice report (Type II & IIIa, IIIb)
- Non-legally binding opinion
- GMCrev: since 2016 involved in
 - switch Rx - OTC status
 - Joint STA-HTA advice and ETA/ETR related advice with RIZIV-INAMI



3: National STA: type of questions

- **Scientific:**

- Quality, non-clinical, clinical
- pharmacovig issues (RMPs, PAES/PASS, Referrals)
- B/R balance
- Unmet medical need / ETA & ETR
- switch Rx to OTC status

- **Technical - regulatory:**

- GMP, GCP, GLP, ...
- regulatory statute of borderline products
- guidelines
- regulatory filing strategy (eg. CTA, SAWP, PIP, MAA, CHMP re-examination, WHO pre-qualification,...)



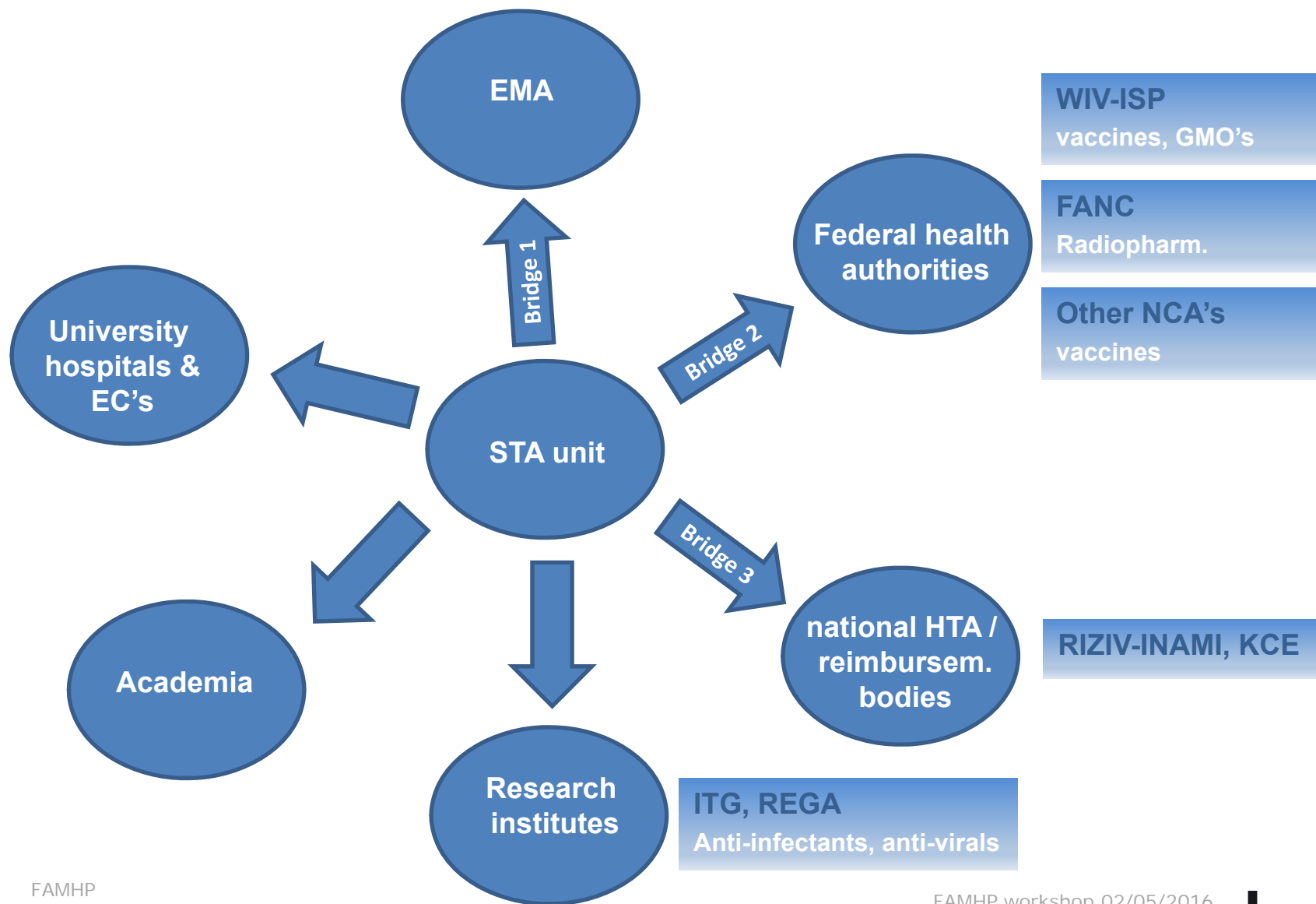
3: National STA: type of questions

- **Other Questions:**

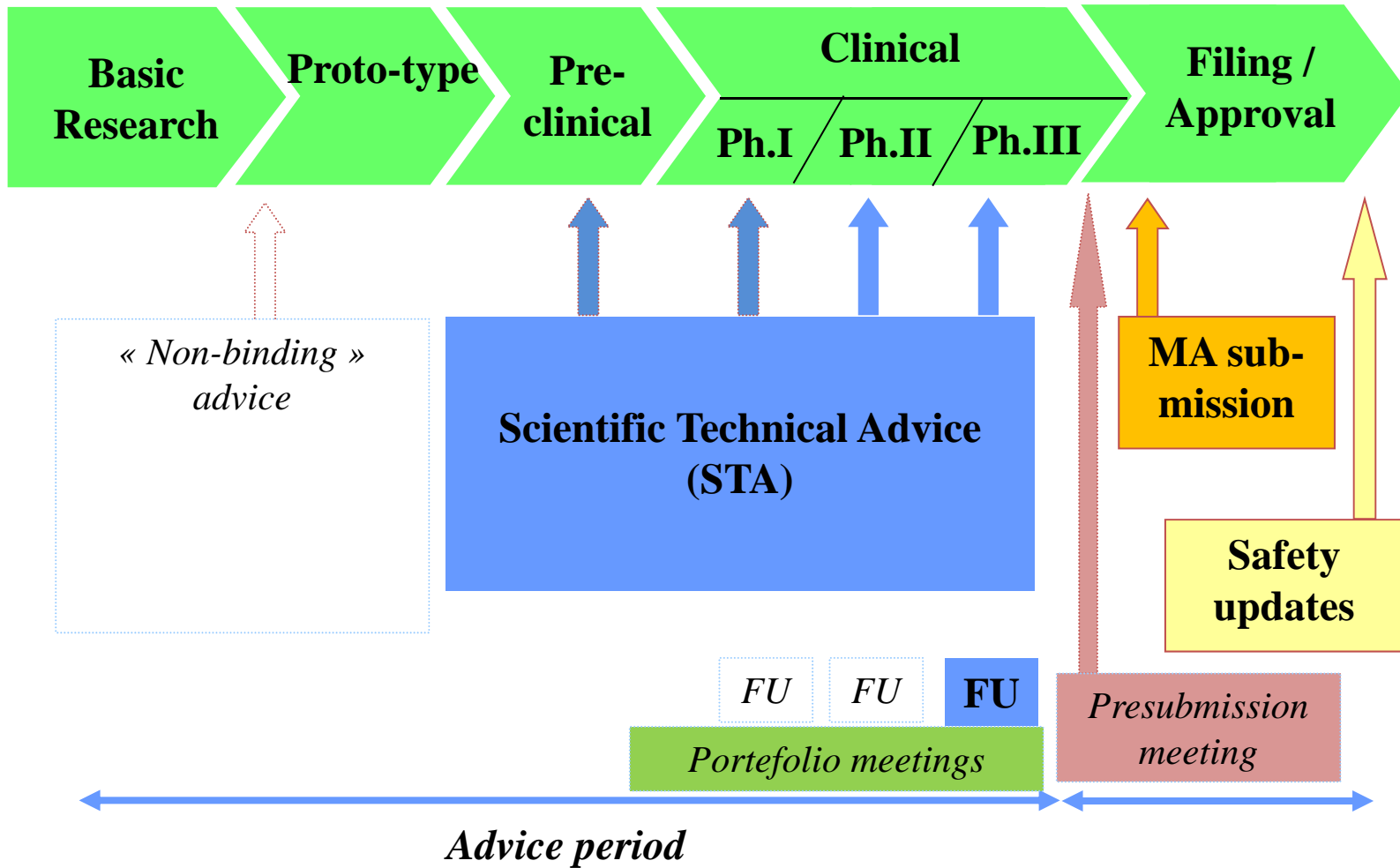
- combination packages
- drug-device combo's (as medicinal product)
- clinical development plans
- (integrated) protocol designs (eg. Adaptive, basket trials)
- New (platform)technologies & concepts (eg. on-site formulation)
- **Joint STA-HTA advice & ETA/ETR related advice with RIZIV-INAMI:**
 - = A valuable tool for facilitating early patient access to highly innovative drug products
 - But: poor uptake in BE



4: National STA: Interaction mechanisms



5: Evolutions in seeking STA: previous situation





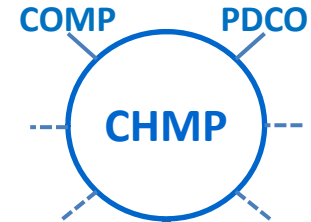
eunetha / Payers

5: Evolutions: TO BE situation



Scientific advice

PRIME



PRAC



Multi-national trials

Earlier in time

Lessons learned - feed-back loop

CURRENT LYFE CYCLE OF MARKETING AUTHORIS. PROCESS

HOW THE PROCESS WILL EVOLVE



STA

Clinical Trials

UMN (CU-MNP)

MAA

Post-Licensing

Commissies voor ethiek

Joint advices

ETA - ETR

CTG



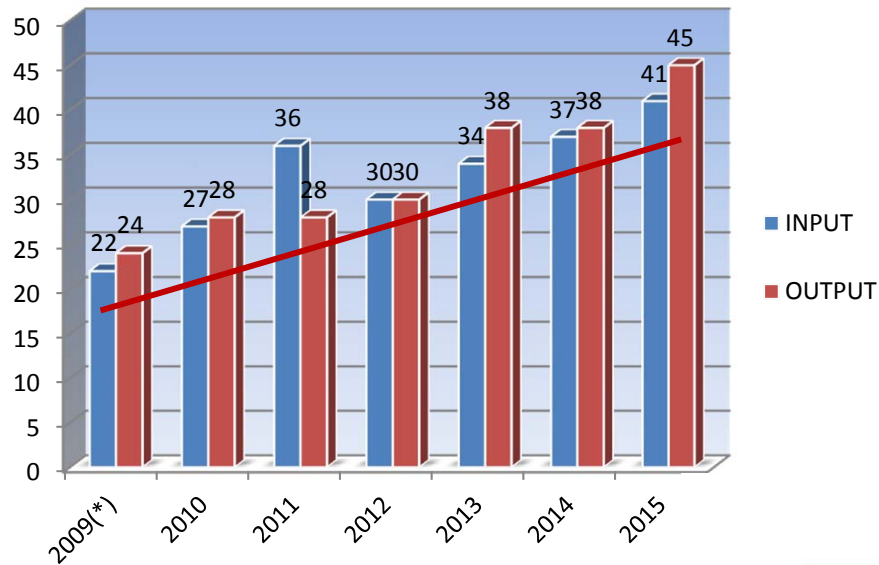
FAMHP afmps-fagg/DGpre authorisation/WTA-KM unit

FAMHP workshop 02/05/2016



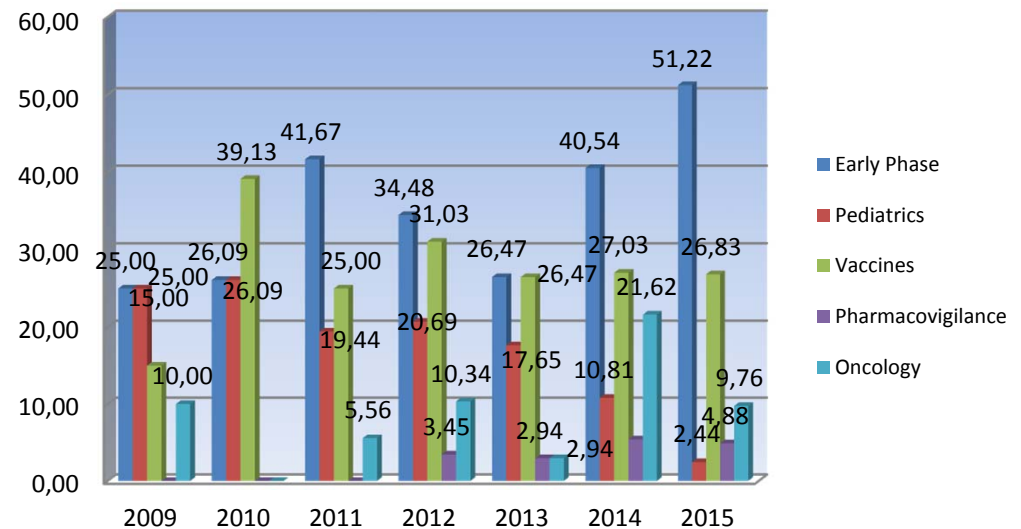
6: National STA: evolutions

Number of STA files



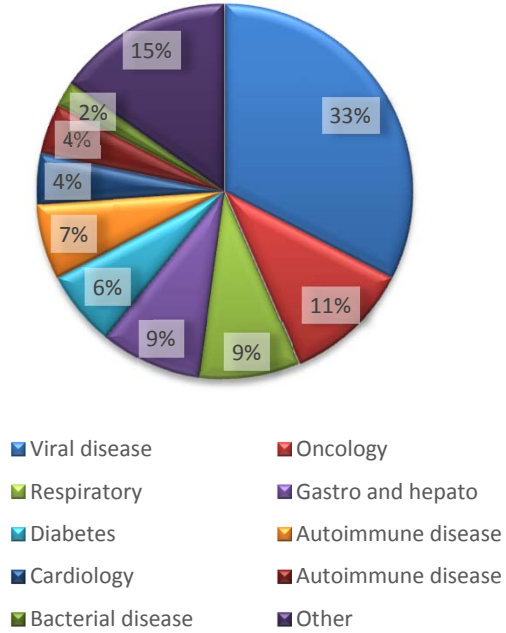
- 2-5 ATMP's / year
- 1 ebola vaccin STA in 2014
- 1 biosimilar STA (onco) in 2013 & 2015

Domain of excellence (%)

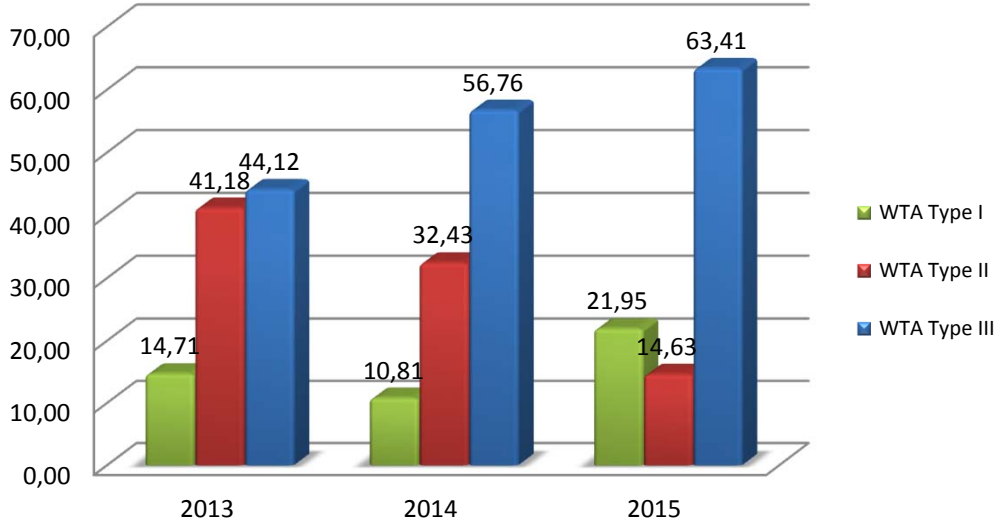


6: National STA: evolutions

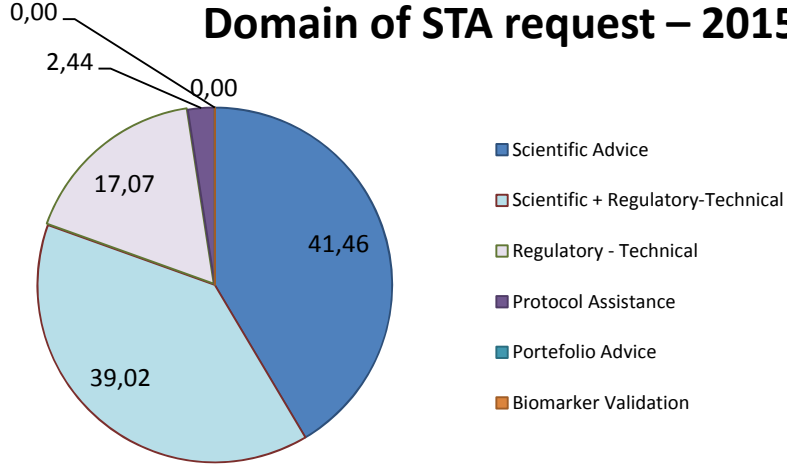
Therapeutic Areas : 2015



Type of STA file (input)



Domain of STA request – 2015 (%)

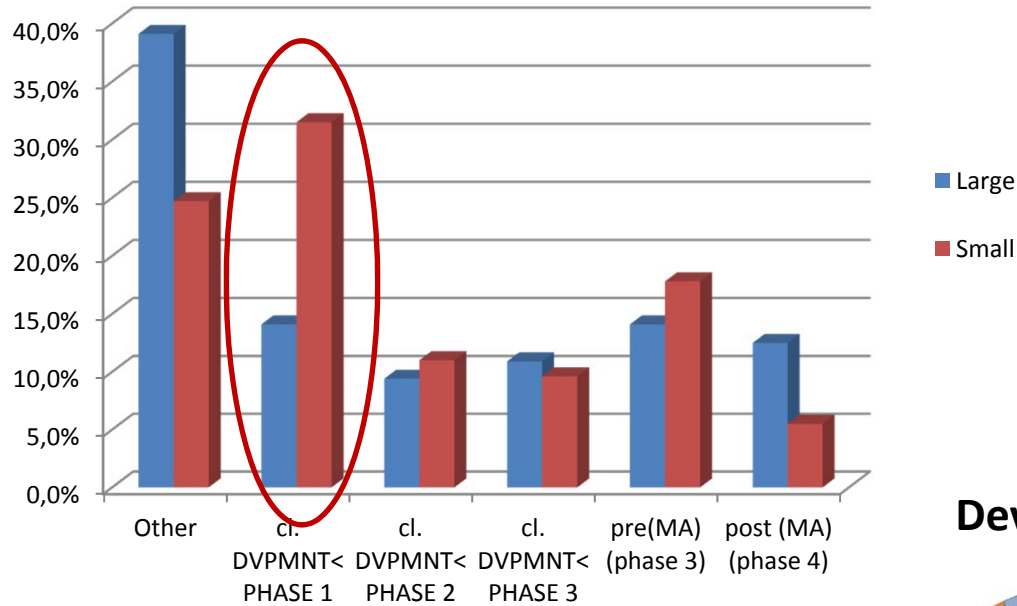


FAMHP
afmps-fagg/DGpre authorisation/WTA-KM unit

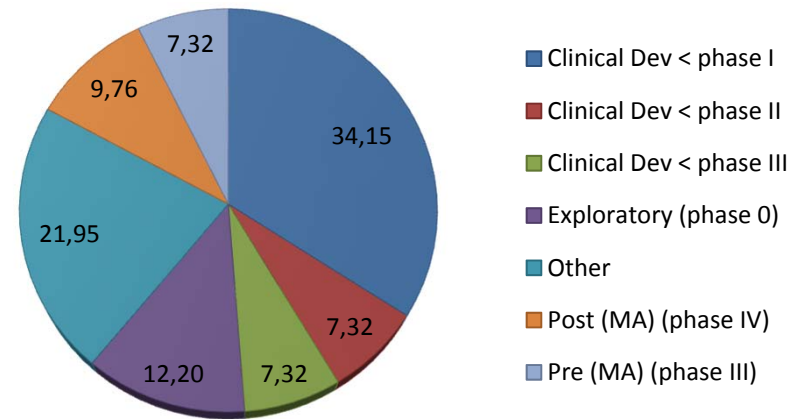


6: National STA: evolutions

Timing of STA requests ifo development phase: 2010 - 2014 (%)

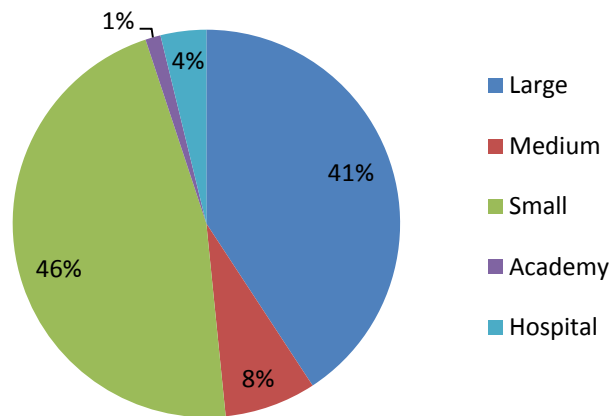


Development phase – 2015 (%)

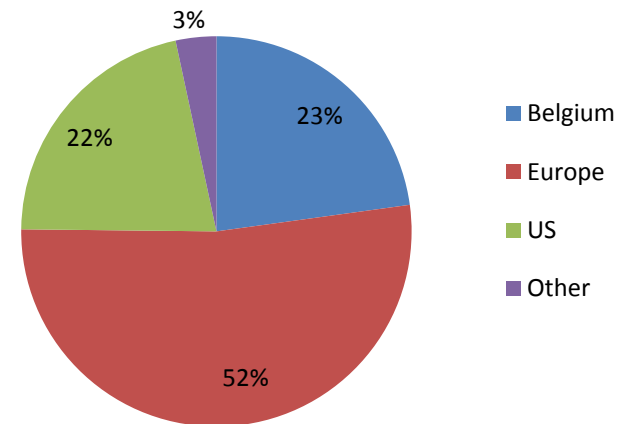


6: National STA: evolutions

**Number of STA 2010-2014:
applicant type (%)**



**Geographic origin of STA
applicants: 2010-2014 (%)**

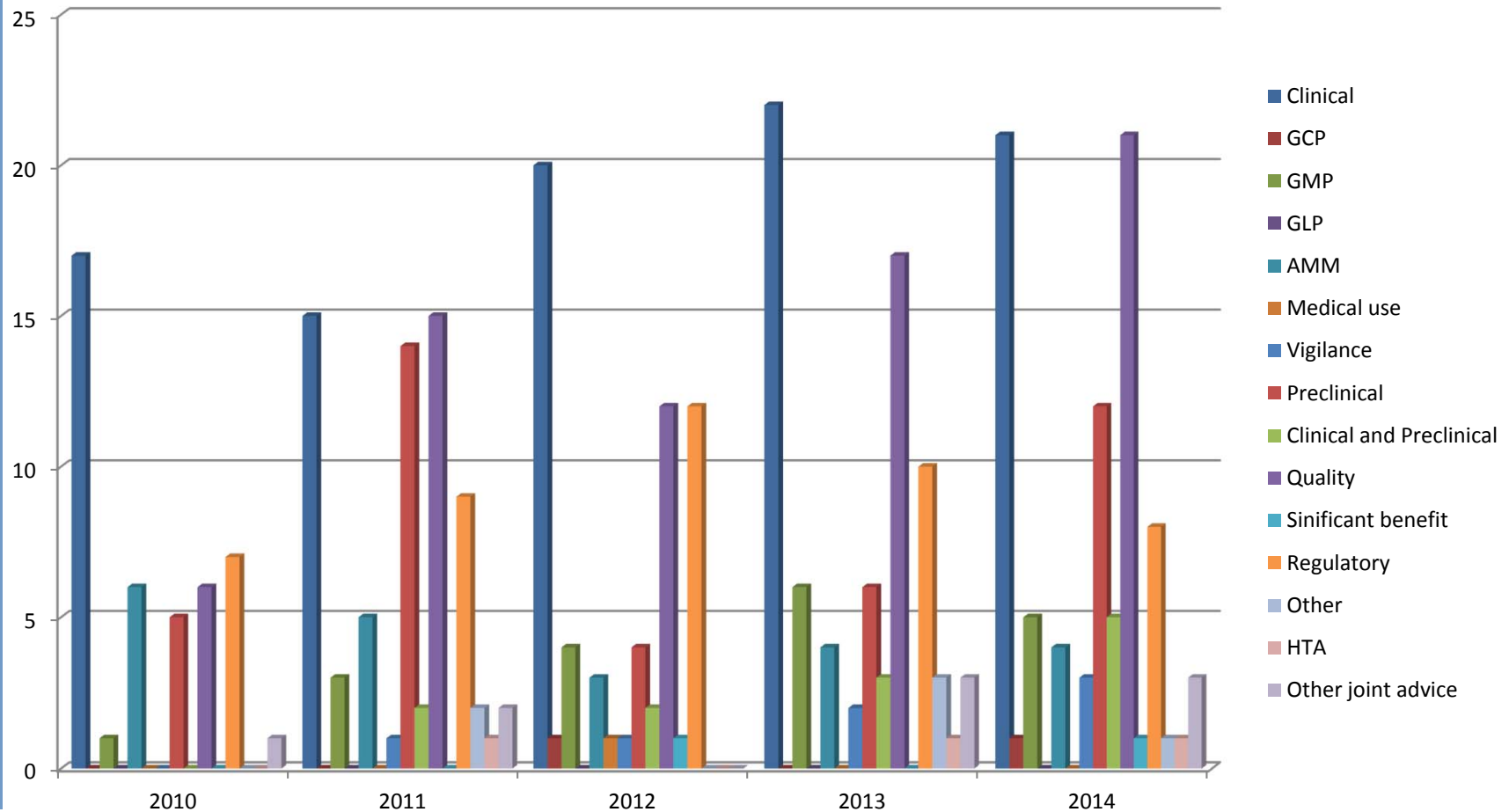


2015	Number	Percentage (%)
# Academics/hospitals	3	6,7
# SME	13	28,9
# Large Pharma	29	64,4
Total STA	45	100,0



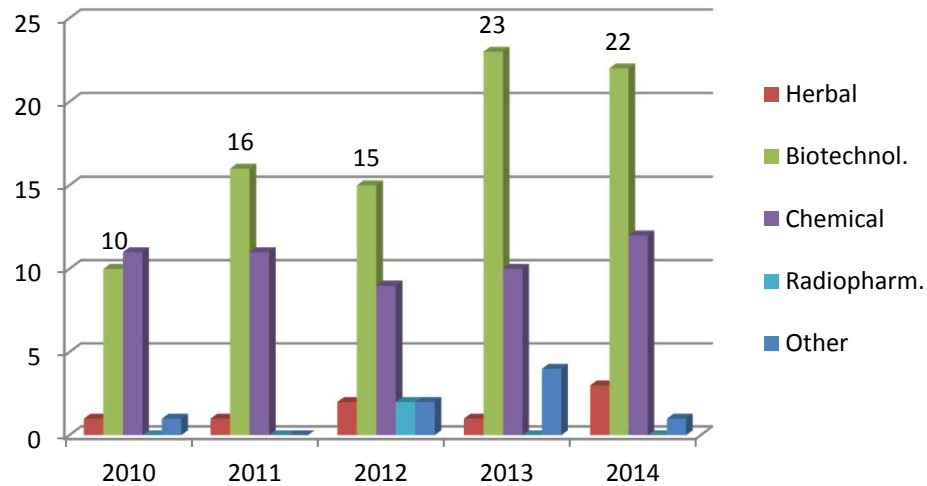
6: National STA: evolutions

Areas of advice / year

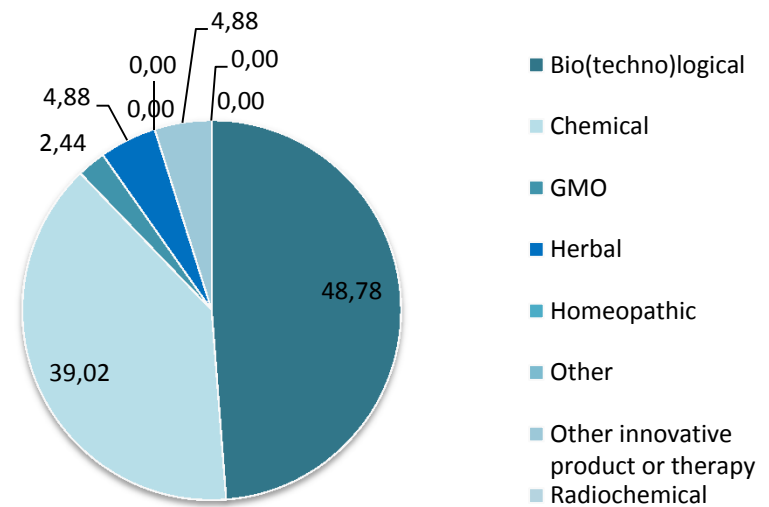


6: National STA: evolutions

National STA - product type

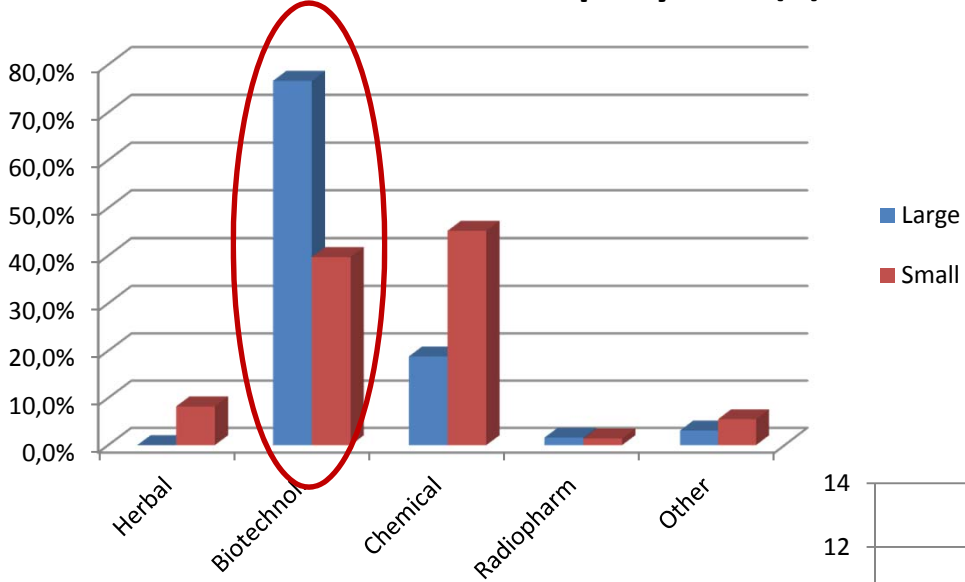


Type of products – 2015 (%)



6: National STA: evolutions in biopharma

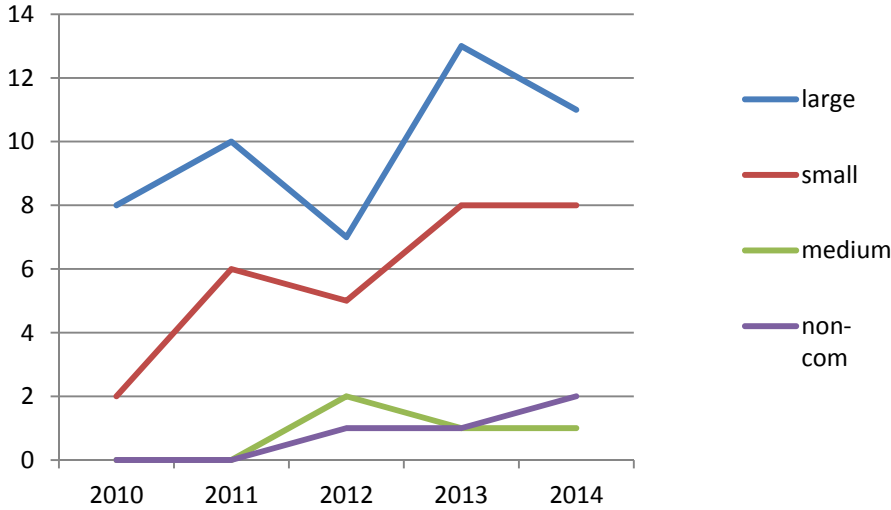
% national STA ifo company size (*)



(*) period: 2010 - 2014

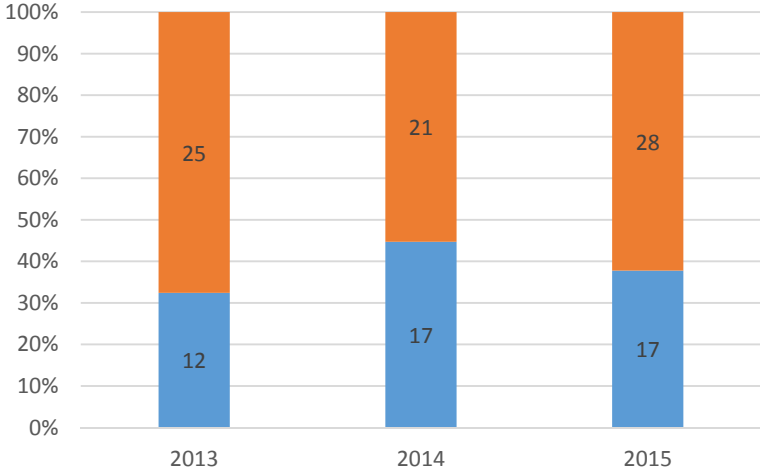


% national Biotech STA's ifo company size



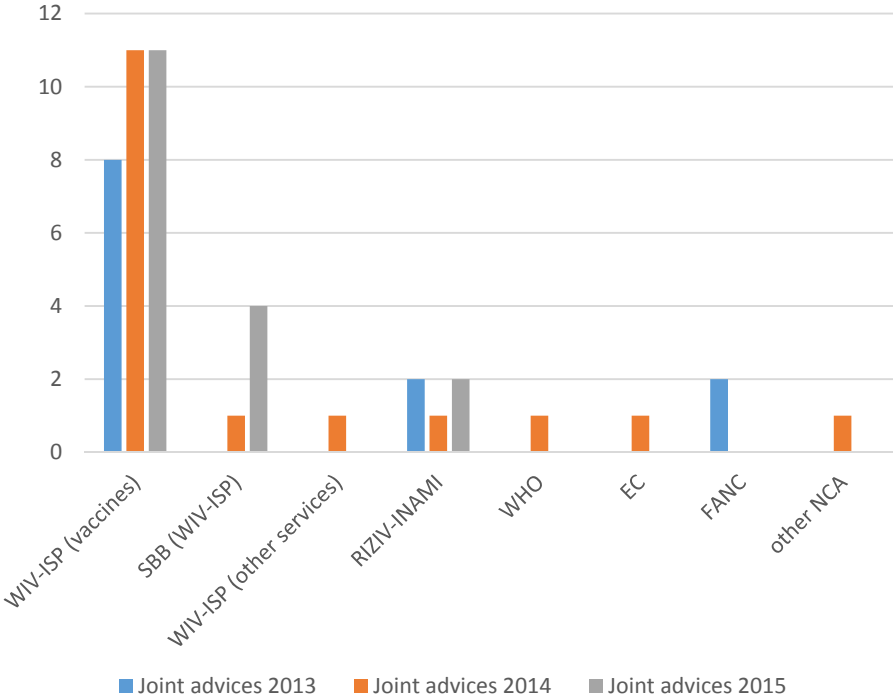
6: National STA: joint advices experience

Joint STA advices (%)



One-stop shop for national STA = key incentive !

Joint STA Advice – involved bodies



6: National STA: joint STA-HTA

INPUT	joint STA-HTA files/year	Total STA files/year	% joint STA-HTA files vs Total	Therapeutic area
2011 (*)	2	36	5,6	oncology
2012	0	30	0,0	NA
2013	1	34	2,9	cardiology
2014	2	37	5,4	Infectio / cardiology
2015	1	38	2,6	oncology
TOTAL	6	175	3,4	

(*) one application was withdrawn by the applicant prior to formal submission.

Main Questions:

- Regulatory aspects (ETA/ETR)
- Unmet medical need
- Added therapeutic value
- Target population
- Product positioning (1st – 2nd line)
- CHMP re-examination
- Standard of care

Key features:

- could be complementary or divergent from EMA views
- more targeted to local situation
- Mainly late stage development



7: European SA statistics:

Number of European Scientific Advices (SAWP-H)

		2014 IN	2014 OUT	2015 IN	2015 OUT
Total number SAWP requests		86	86	93	91
According to procedure	Scientific Advice	81	81	92	90
	Qualification procedures & HTA	4	4	1	1
According to spearhead domain	VACCINES	4	6	9	9
	EARLY PHASE DEVELOPMENT	1	2	8	8
	ONCOLOGY	24	25	13	13
	BIOSIMILARS	N/A	N/A	8	8

Number of European Scientific Advices (SAWP-V)

		2014 IN	2014 OUT	2015 IN	2015 OUT
Total number SAWP requests		1	1	5	2
According to procedure	Scientific advice	1	1	5	2
According to spearhead domain	VACCINES	NA	NA	2	0



8: Portfolio meeting & FAQ's: statistics

Number of portfolio meeting requests

Type of Portfolio Meeting	2013	2014	2015	Q1-Q2 2016 (*)
General	1	2	1	5
Vaccines	1	2	1	0
Oncology	1	2	1	0
Early phase development	0	0	0	1
ATMP's	0	0	0	1
TOTAL	3	6	3	7

(*) 5 closed + 2 ongoing

Number of FAQ's

	2014	2015
FAQ's received	125	166
Response delay < 5 days	92%	94%
Response delay > 5 days	8%	6%

Early informal dialogue & guidance is needed prior to formal STA !

= 32,8 % increase



9: Importance of national STA for applicants & patients

- Facilitation & acceleration of (pre)clinical research in Belgium & EU
- Preventing expensive, time-consuming, unnecessary or unethical clinical research
- Better follow-up of product life cycle
- Building up robust data
- Constructive guidance prior to formal submissions
- Earlier availability & access of new, innovative drug products to patients



10: Advantages of national STA from FAMHP

- easy access to support & guidance prior to formal STA submission
- vast array of scientific & regulatory questions
- combination of both scientific & regulatory-technical questions
- joint advice with other NCA's possible when needing complementary expertise: RIZIV, WIV, FANC, ...
- reasonable timeframe & predictive timelines
- access to external networks of expertise
- strong interface with belgian EU representatives at EMA (eg. SAWP, CHMP, CAT), CMDh, CTFG, ...



11: Maximizing the benefit of national STA

- come early in development
- seek pre-submission guidance if first time
- ask specific questions – (no limit in nr. of questions)
- present concise and comprehensive data in a structured format (eg. CTD)
- carefully prepare the STA submission (questions, company position, regulatory strategies,...)
- raise the right questions!
- approach the advice meeting in an open manner
- consider the need for FU advice



Impact on succes rate on future filing !



12: SME & academia-related STA challenges

- STA procedures/advantages not well-known
- SME incentives insufficiently known, dispersed or lacking (international - EU - national level)
- STA fees = financial hurdle !
- STA file preparation: resources lacking
- Identify & define critical STA questions
- Different SME definitions!
- SME's & academia: a very heterogenous stakeholder group
- TTO's = a critical interface!



13: Future initiatives & challenges

- Optimisation of STA procedures & interaction with GMCrev
- joint STA-HTA & ETA/ETR related advice: building up expertise & credibility at BE & EU level
- New National STA procedures for:
 - medical devices:
CI's and evaluations, drug-device combo's, consultation procedure for NBs, etc.
 - borderline products: regulatory statute and classification issues: CTA ↔ CI route
 - Regulatory advice on existing legislation & guidelines



13: Future initiatives & challenges

- Building up support & guidance for SME's, academic spin-offs, (university) research centres:
Close the gap: basic R&D → applied, clinical research
- Exploring new support mechanisms for stimulating pharmaceutical R&D & innovation in Belgium for the patients' benefit
- Future involvement in: **The Innovation Offices Network (EU-IN), a new tool in the EU medicines agencies network strategy for seamless support to Innovation**
- Preparing the ground for a national innovation office !



STA info & guidance at FAGG website

The screenshot shows the FAMHP website interface. The main navigation bar includes 'Human medicines', 'Veterinary medicines', 'Information for the public', and 'Notification of adverse reactions or incidents'. The 'Human medicines' section is active. The breadcrumb trail reads: Home > Human medicines > Medicines > Medicines > Scientific-technical advice. The left sidebar lists categories: Medicines (Homeopathic, Herbal), Health Products (Medical devices, Human body material, Blood), and Particular products (Raw materials). The main content area is titled 'Scientific-technical advice' and lists links: Introduction, Procedures, Regulation, Fees, and FAGG. A red oval highlights a workshop announcement: 'Workshop "National & EU scientific regulatory support mechanisms and initiatives for innovation in drug development" - 2nd May 2016'. Other featured content includes '5-year celebrations at famhp!', 'Notification of adverse reactions or incidents', and 'PIL and SPC of a medicine'. The browser address bar shows the URL: http://www.fagg.be/en/human_use/medicines/medicines/s. The Windows taskbar at the bottom shows the date 24/04/2016 and time 10:49.

http://www.fagg-afmps.be/en/human_use/medicines/medicines/scientific_technical_advice/



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A large, stylized graphic of a human eye, rendered in light gray and blue tones, serves as a background for the central text. The eye is composed of a large, light gray arc at the top, a smaller, light blue arc at the bottom, and a central white circle representing the pupil. The text is centered within a dark blue rectangular box that overlaps the eye graphic.

**Vos médicaments et produits de santé,
notre préoccupation**

**Uw geneesmiddelen en
gezondheidsproducten, onze zorg**