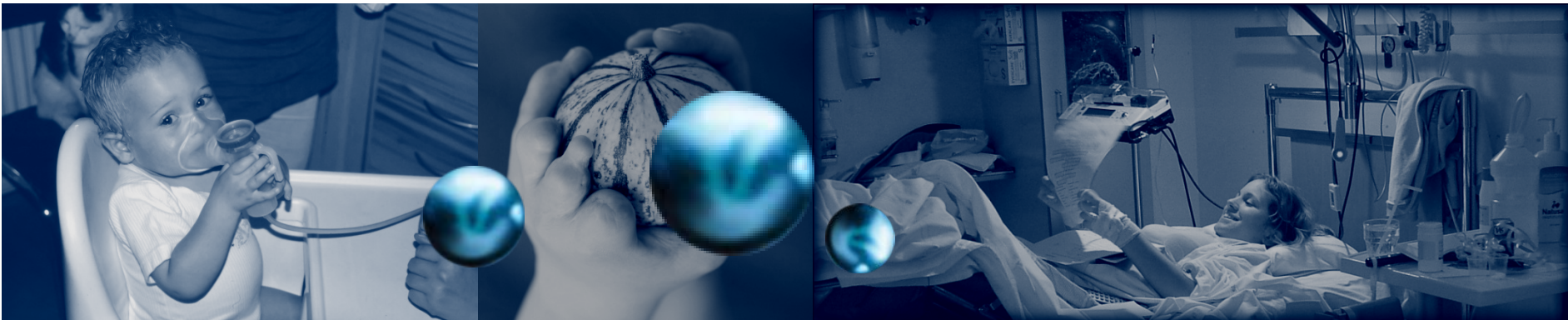


Understanding off-label use and the information needs of patients: a pilot Eurordis survey in rare diseases



Drug Information Transparency and Access (DITA) Task Force

Compiled by Rob Camp and Richard West
EMM Dubrovnik; 30 May-01 June 2013



Background

- 4000 to 6000 distinct rare diseases
 - Defined as $<1/2000$ or $<250,000$ patients EU-wide
 - 4-6% of EU population affected
- More than 1000 OMP designated
 - Of which 71 are authorised for 83 rare indications
- Most patients with a rare disease are not treated with an authorised orphan medicine
 - when they are treated
- Off-label use is the rule, not the exception in RD
- 18% of patients with a RD rejected by HCP
 - 85% due to disease complexity (EurordisCare 3 survey)



One example



- Jenny's parents' garage
- In infancy, J was diagnosed with cystinosis
- Medically, she suffered renal failure by the age of 6 (+ hypothyroidism, insulin-dep. diabetes, hepato-splenomegaly with hypertension, muscle and cerebral involvement, photophobia)
- Her parents refused to sit idly by
- They contacted pharma companies
- They learned how to treat their child “off-label”, where nobody had been before
- Getting information directly from the company was life-saving
- Jenny received daily dialysis until age 22
- Her parents created Climb, the National Information Centre on Metabolic Diseases in the UK, so children like Jenny can live longer



Objectives

Document patients' experience with OL use

Learn about the information patients receive

Create database of off-label uses in rare diseases

Explore how patients handle ADRs with OL use

Define future actions on OL use in rare diseases

OL: Off-label

ADRs: Adverse Drug Reactions



90 conditions, 105+ off label uses

Condition	Product	Indication	Off label use
Dravet syndrome	Urbanyl	Epilepsy, but not recommended for use in children between the ages of six months and three years	5 mg twice a day since the age of 6 months. With micropakine, diacomit, epitomax
Friedreich Ataxia	Idebenone	Alzheimer's disease and other cognitive defects	720 mg/day for 12 years
Behcet disease	Thalidomide	Multiple myeloma	1 mg/kg/week to 1 mg/kg/day

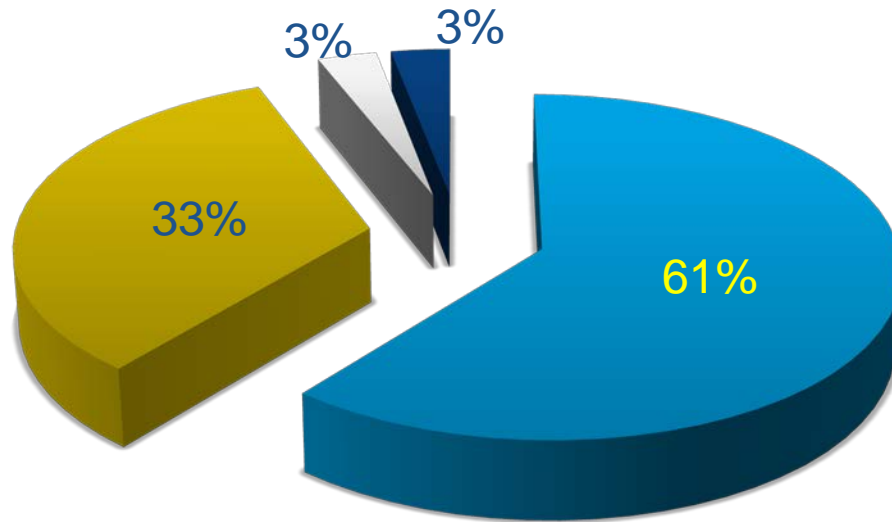


Methodology

- Online survey, 5 languages
- Short description on what is off-label, why we were doing the survey with (18) questions
- Open for 2 months (Eng) or 1 month (other languages), May-Jul 2012
 - One reminder sent in all languages, two in Spanish
- Developed by DITA at Eurordis from Nov 2010
- Target population – people with rare diseases who had used drugs off-label in the past



Who answered our survey?

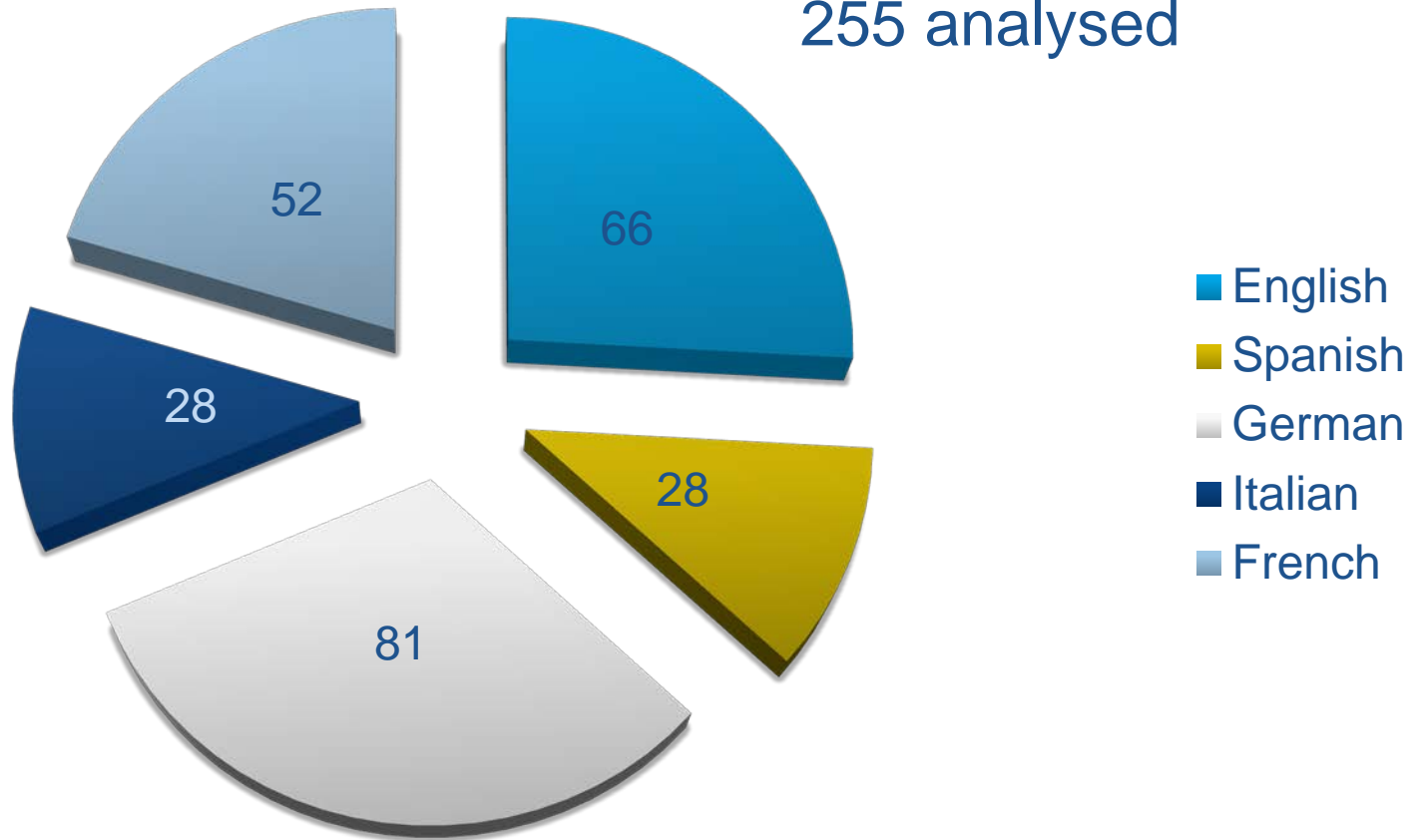


- The person taking the treatment
- A parent
- Another family member
- Another care provider



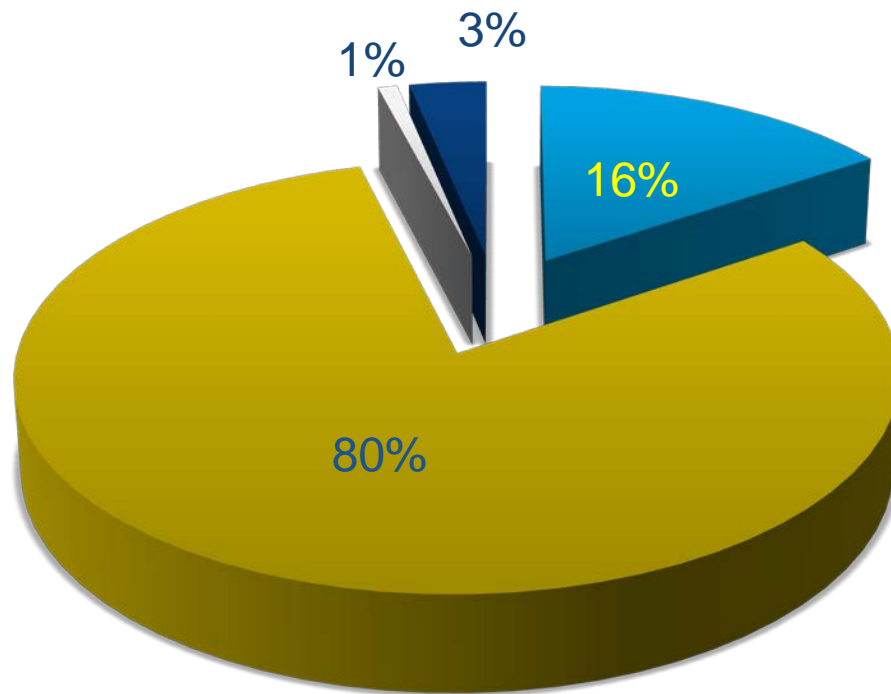
Respondents' language

294 responses received
255 analysed





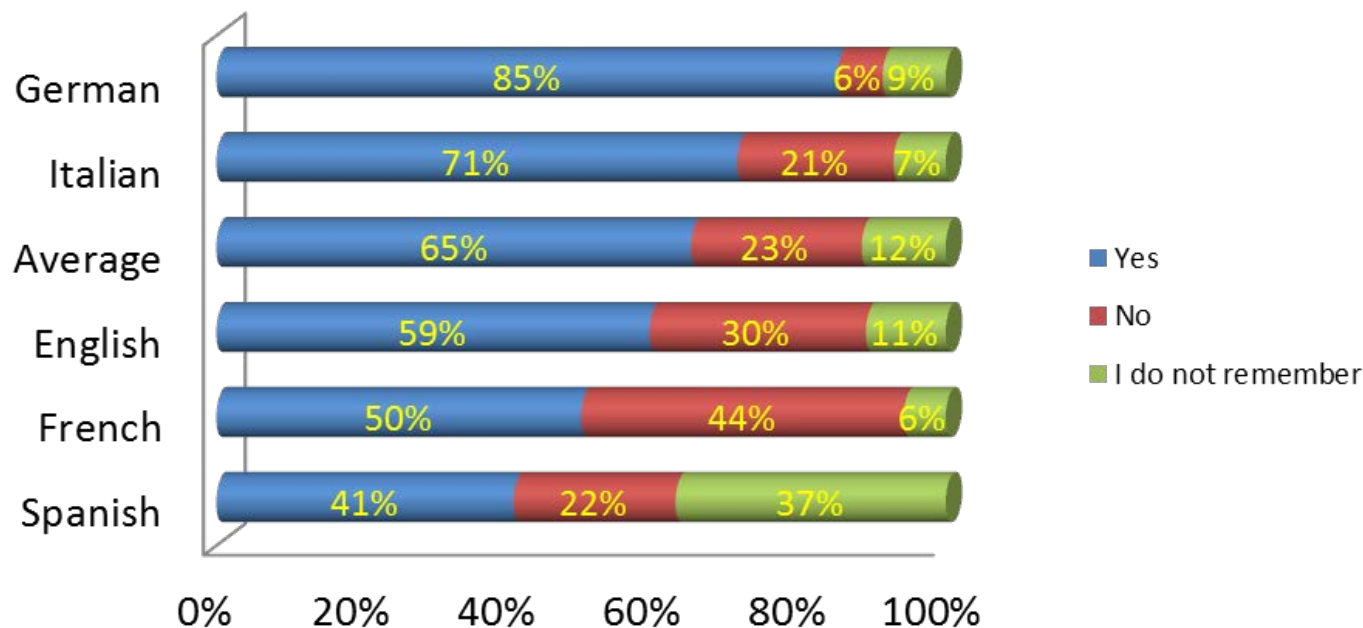
Who proposed the (OL) use?



- I did
- The doctor
- I don't remember
- Another professional



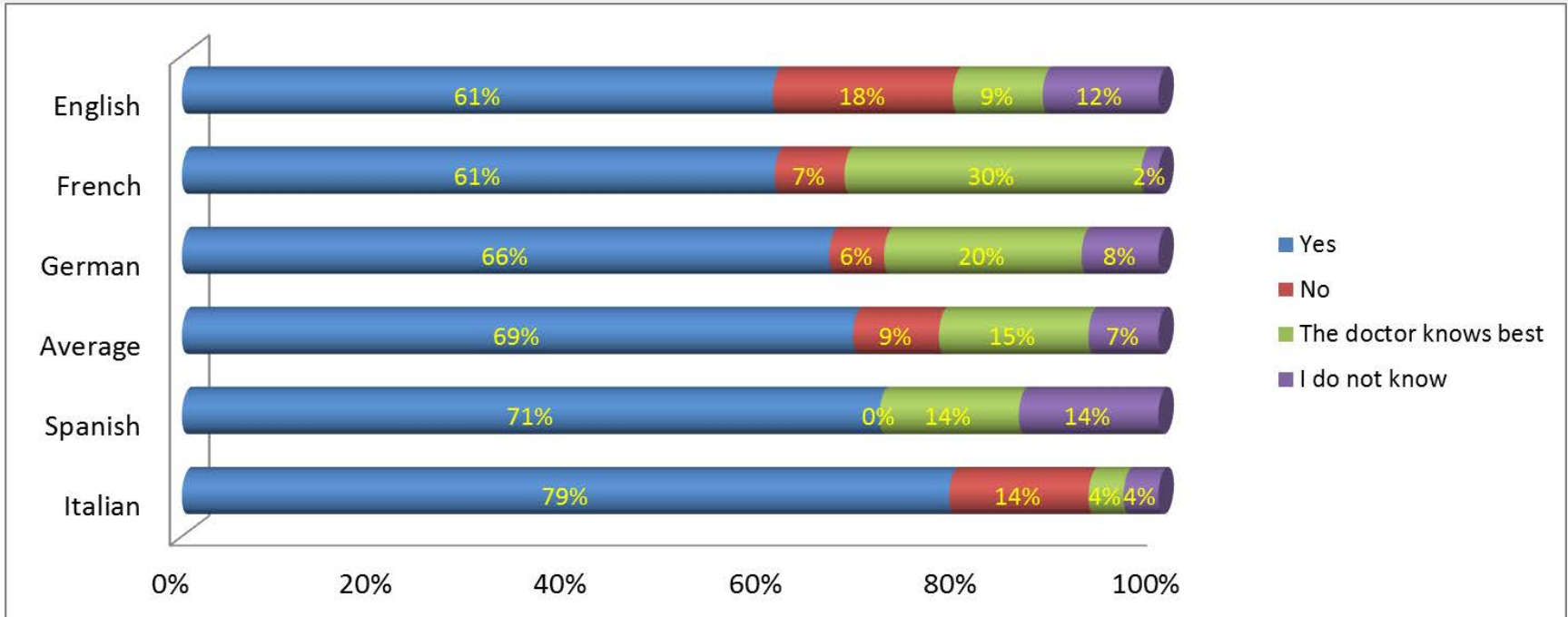
Was it explicitly discussed that the drug was off-label?



	Yes	No	I do not remember
German	69	5	7
Italian	20	6	2
English	38	19	7
French	26	23	3
Spanish	11	6	10
TOTAL	164	59	29



Should there be more explanation about risk/benefit?



	Yes	No	The doctor knows best	I do not know
French	34	4	17	1
English	46	14	7	9
German	59	5	18	7
Spanish	20	0	4	4
Italian	22	4	1	1
TOTAL	211	27	47	22



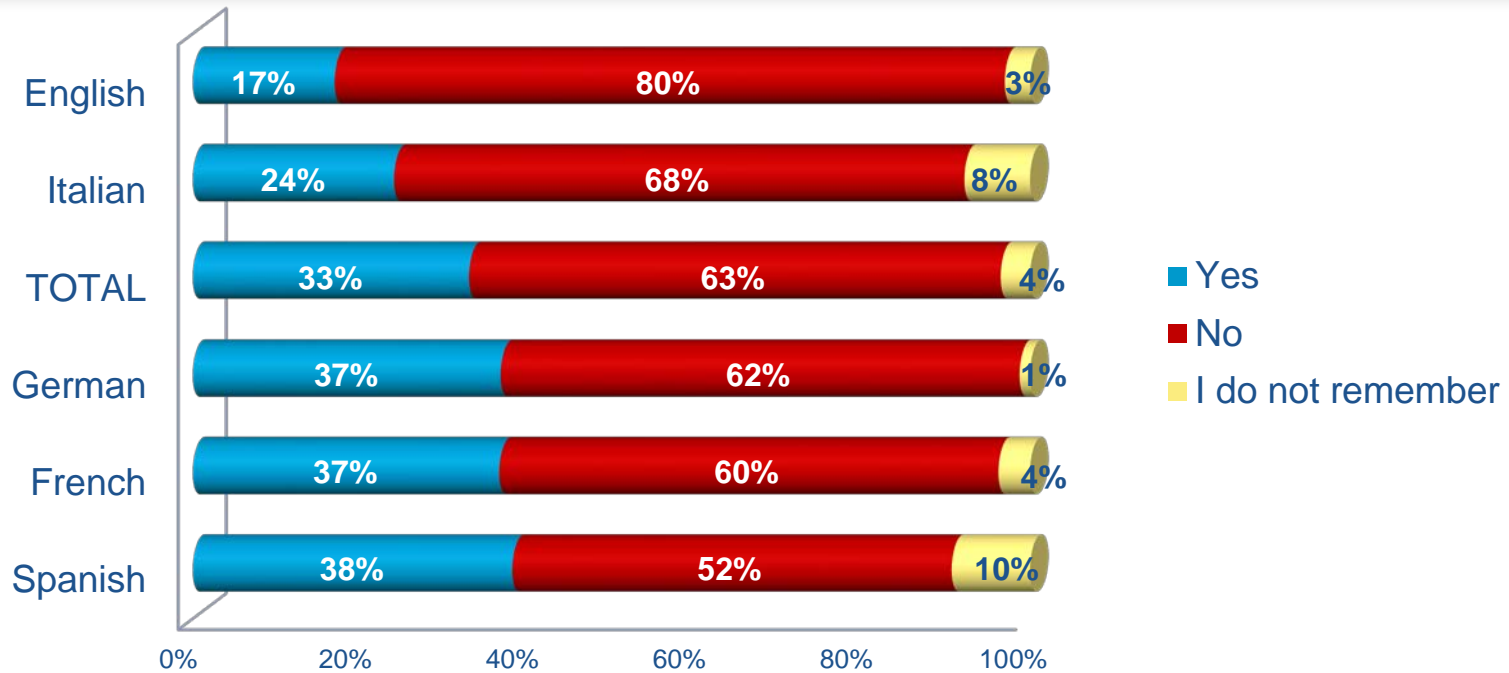
Common “more explanation” comments



- ...the side effects are what patients should be told about, and how severe (they may be)
- We did not know it was an off-label indication until my father went blind due to the drug
- Helpful – a phone line, email link, Internet research, signed written consents
- The doctor was very clear, I understood it all...
- I find myself desperately accepting whatever the doctor offers...
- Doctors do not know everything



Were there adverse events while taking the drug?



	Yes	No	I do not remember
English	11	52	2
Italian	6	17	2
German	29	49	1
French	19	31	2
Spanish	8	11	2
TOTAL	83	160	9

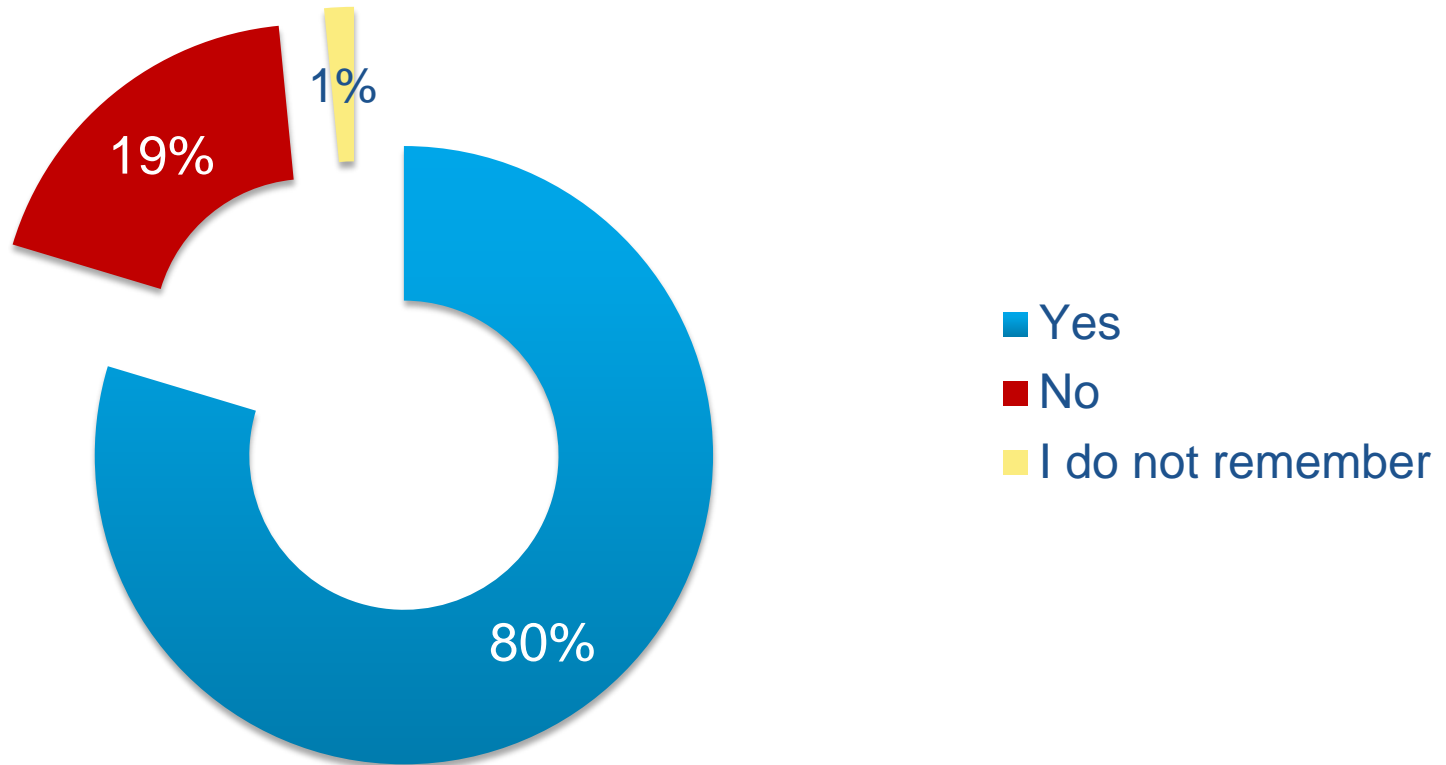


Adverse events descriptions

- ...it did incapacitate my abilities of clear and rapid thinking permanently, it produces a mental blockage and intracranial pressure. It also caused constipation and/or diarrhoea.
- (there has been a drop) in my blood platelets, haemoglobin and red cells. I have required various transfusions of platelets and red corpuscles
- the copper ... gets deposited in the brain, he was temporarily incapacitated, ... was hospitalised and now has some sequelae
- Severe aches, itching, headaches, dizziness and hyper-sex drive which continued for approx 5 years - never investigated by a health professional or even warned (about them)...
- Tunnel vision, lack of coordination, frequent falling, impaired brain function, blackouts. While driving home from work, I blacked out in the car for several seconds.
- Nerve end damage to my fingers and feet. Pins and needles in my feet and hands. I was violently ill, throwing up, fever, rash - no permanent damage

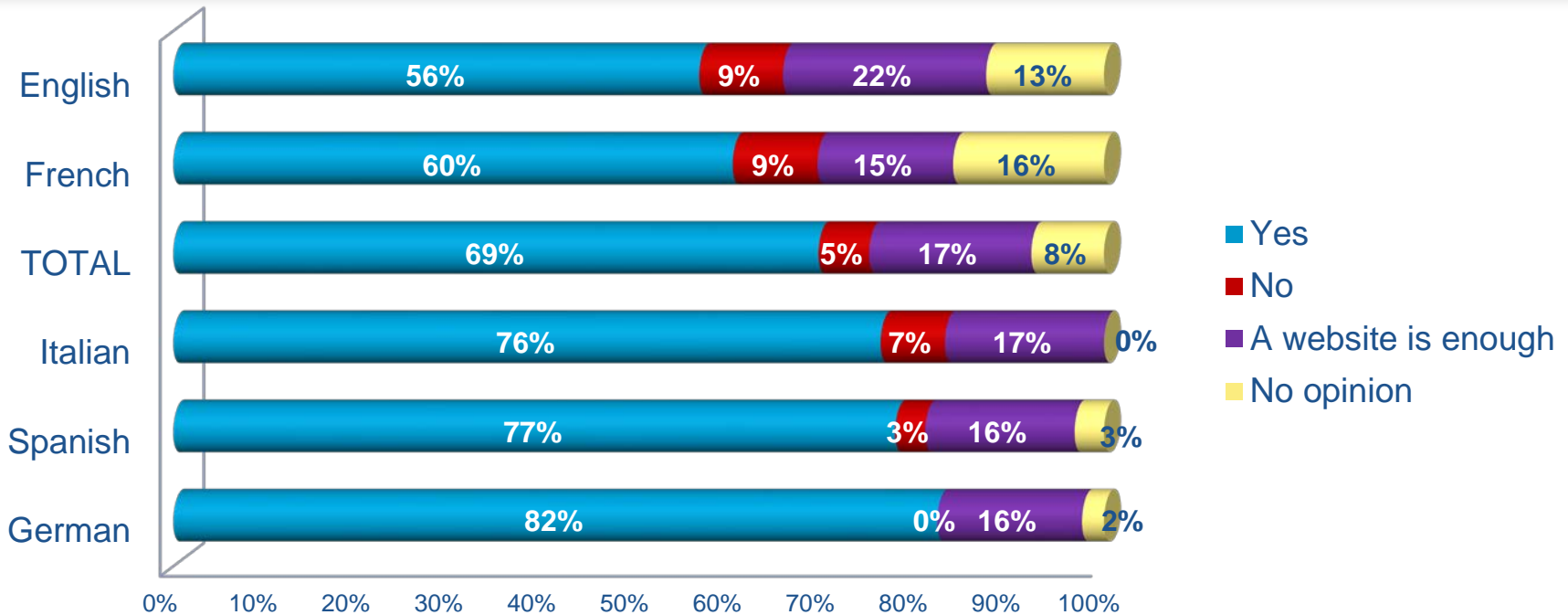


Did you report the adverse event?





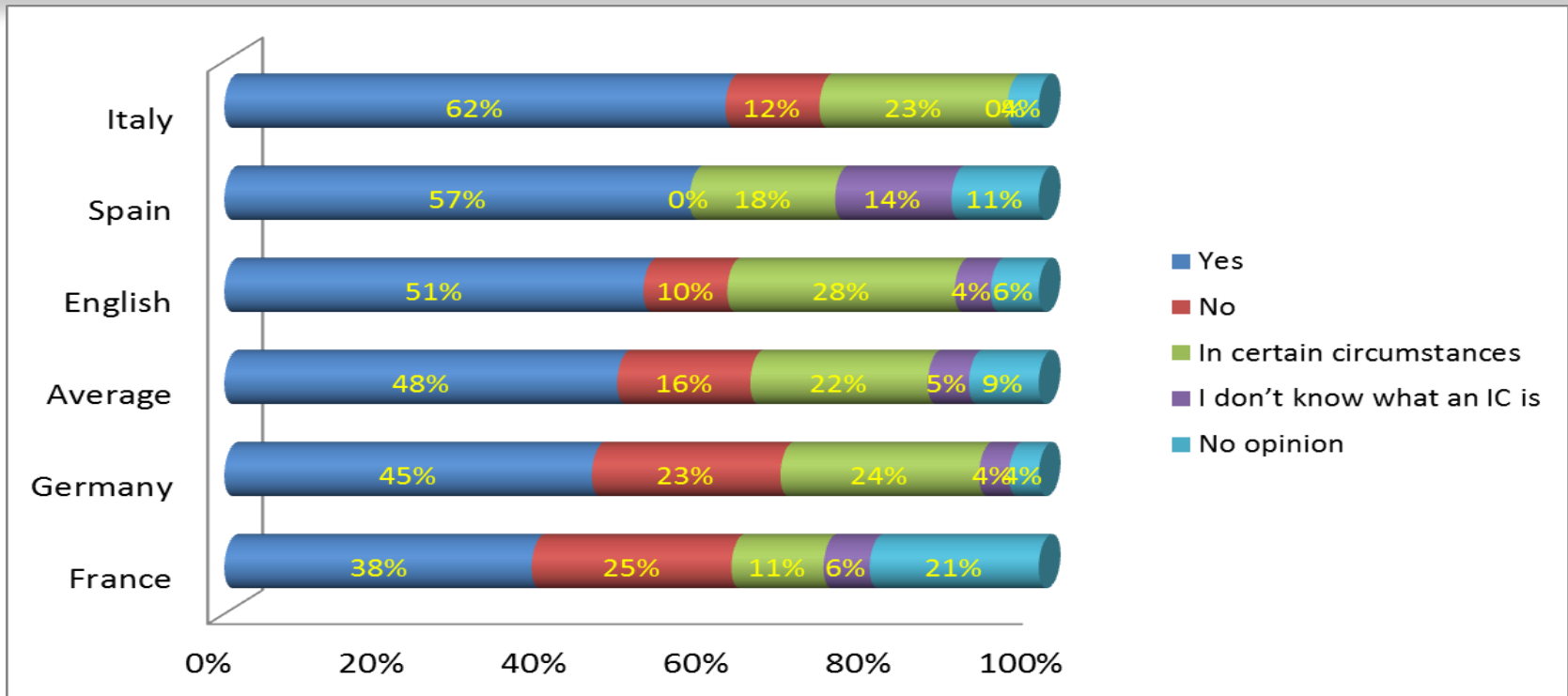
Should there be a dedicated help line to report side effects?



	Yes	No	A website is enough	No opinion
English	44	7	17	10
French	33	5	8	9
Italian	22	2	5	0
Spanish	24	1	5	1
German	68	0	13	2
TOTAL	191	15	48	22



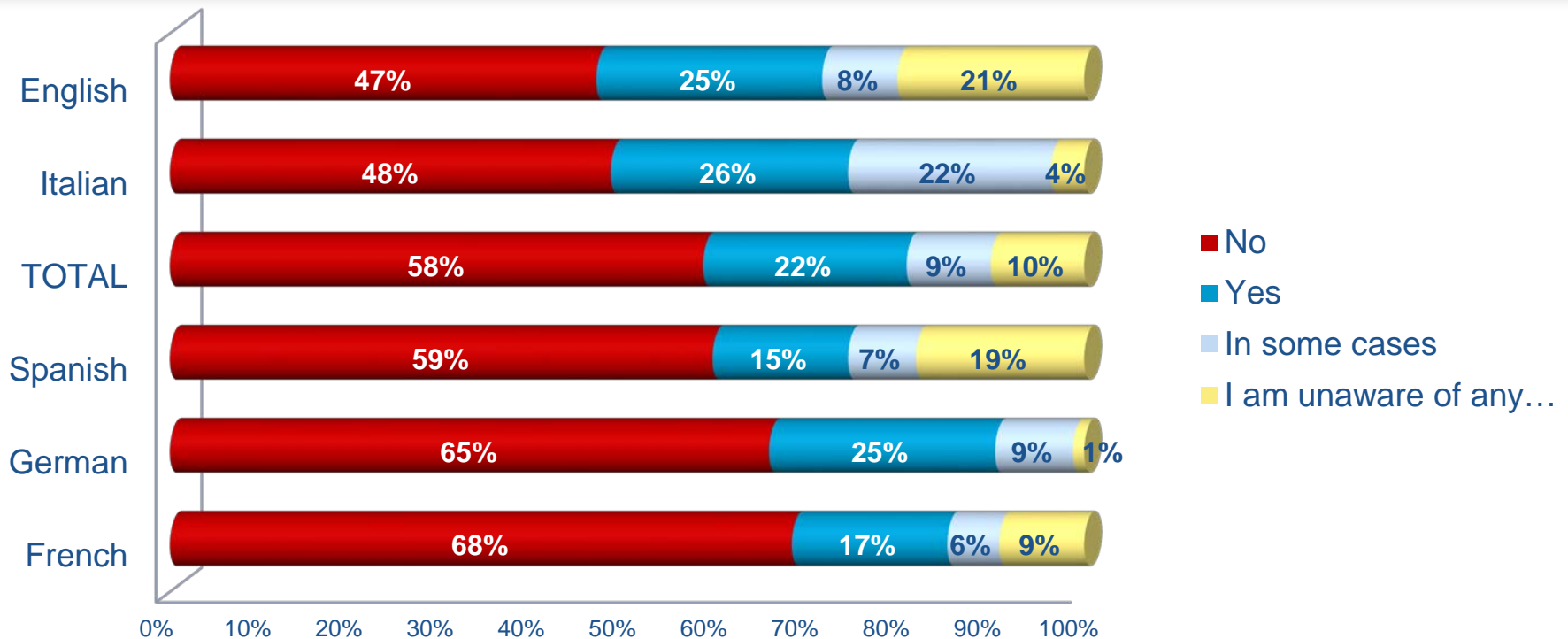
Should an informed consent form be required for off-label?



	Yes	No	In certain circumstances	I don't know what an IC is	No opinion
Italian	16	3	6	0	1
Spanish	16	0	5	4	3
English	35	7	19	3	4
German	37	19	20	3	3
French	20	13	6	3	11
TOTAL	124	42	56	13	22



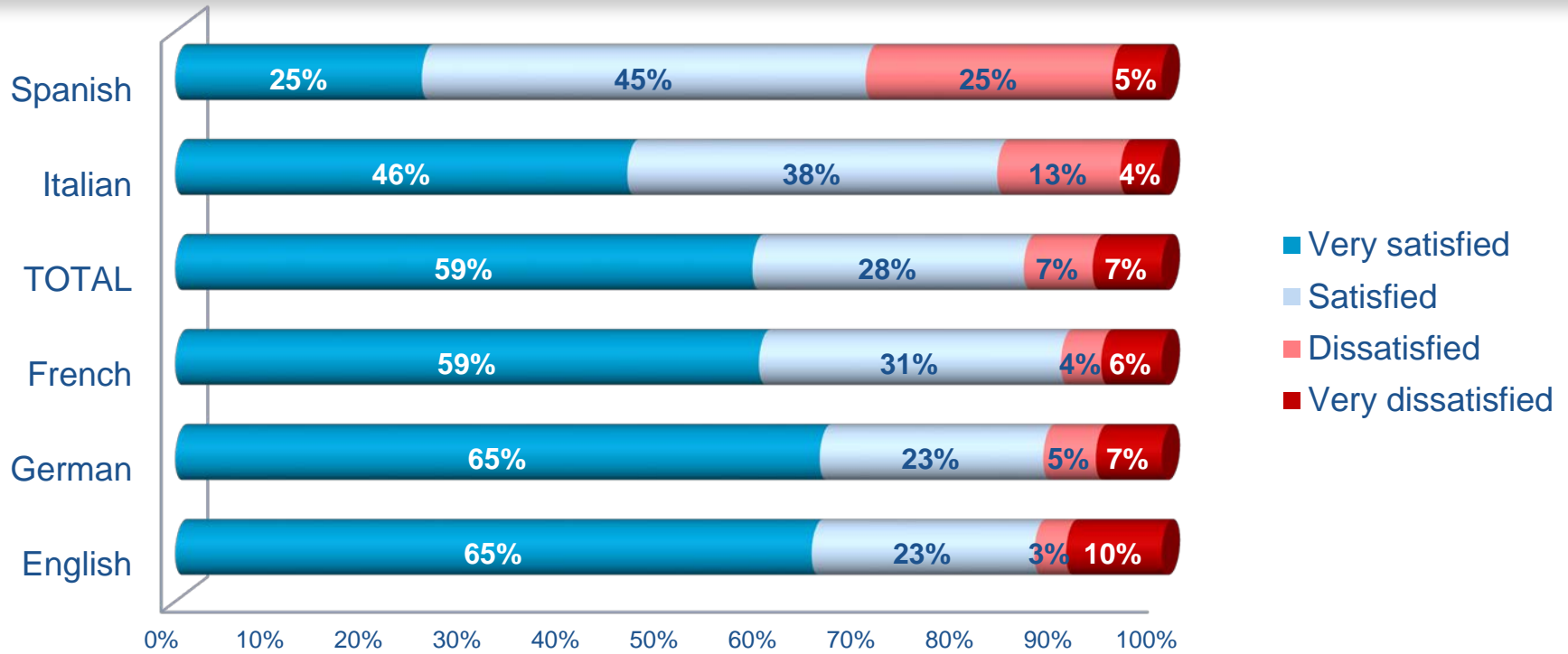
Were there any supply or reimbursement issues?



	Yes	In some cases	No	I am unaware of any...
English	18	6	34	15
Italian	7	6	13	1
Spanish	4	2	16	5
German	20	7	53	1
French	9	3	36	5
TOTAL	58	24	152	27



Your rating of the off-label experience



	Very satisfied	Satisfied	Dissatisfied	Very dissatisfied
English	40	14	2	6
Spanish	5	9	5	1
German	49	17	4	5
Italian	11	9	3	1
French	29	15	2	3
TOTAL	134	63	16	16



Your OL experience

- There aren't many specific treatments and there is not a lot of research because it isn't money-making for the big pharma companies, (so) other drugs do help alleviate some of the symptoms, although they are not indicated, and as long as they explain about the risk/benefit, it (*the OL*) seems fine to me
- It (*the treatment*) seems to be working
- The treatment has given me 18 months remission and I have not had to take any other medication since my treatment
- I do think that records should be kept of off-label usage so they can be collated to inform both medics and patients of the success or otherwise of the drug ...
- Depends on the drug – some are failures, others work well
- No significant changes, the condition is not getting worse
- It worked but there are lots of side effects



Discussion

- Patients' and doctors' ability to communicate fully is limited
 - OL risks can be ameliorated by fuller communication at all steps in the therapeutic process
- Patients' understanding of OL is limited
- Types of adverse events here are significant – even when only 1/3 experience them, those who do have stories to tell
- The less information/understanding of OL, the less comfortable with OL & their treatment a person may be
 - Does this also coordinate with comfort of being able to share with your doctor?
- Patients need and want more (and better) treatments
- Patients need and want more information
 - How can this be done?



Off-label

- Back up slides

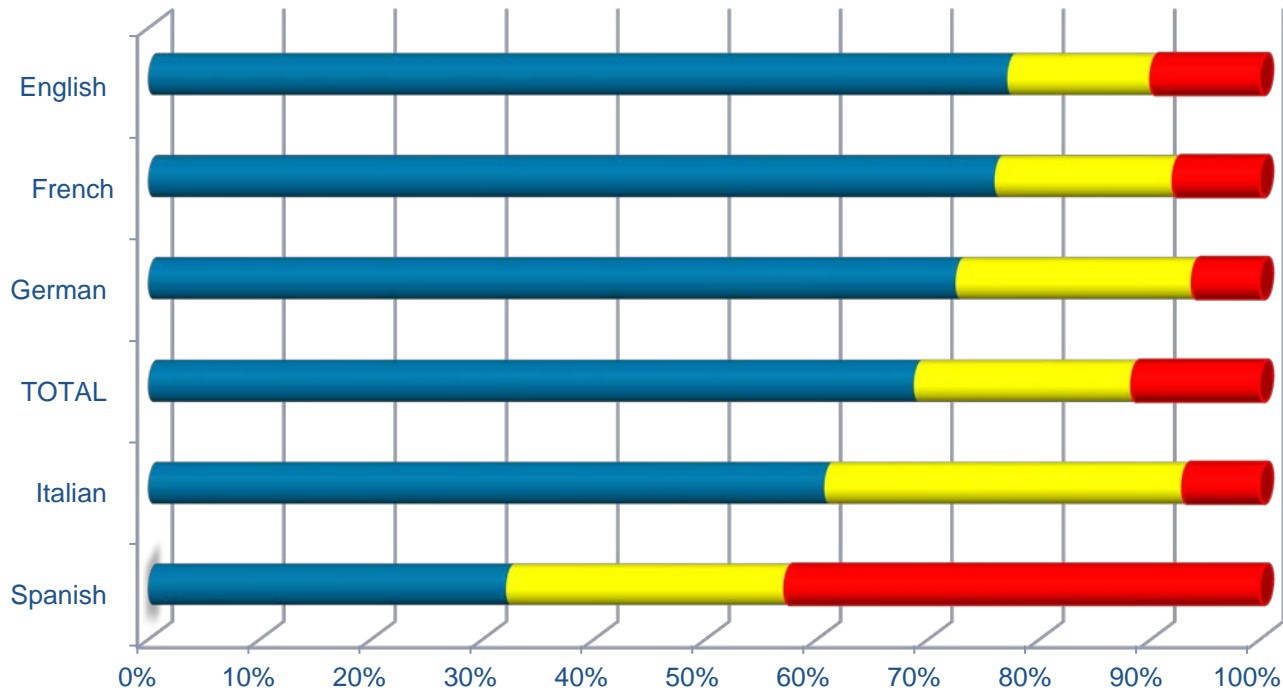


90 conditions, 105+ off-label uses

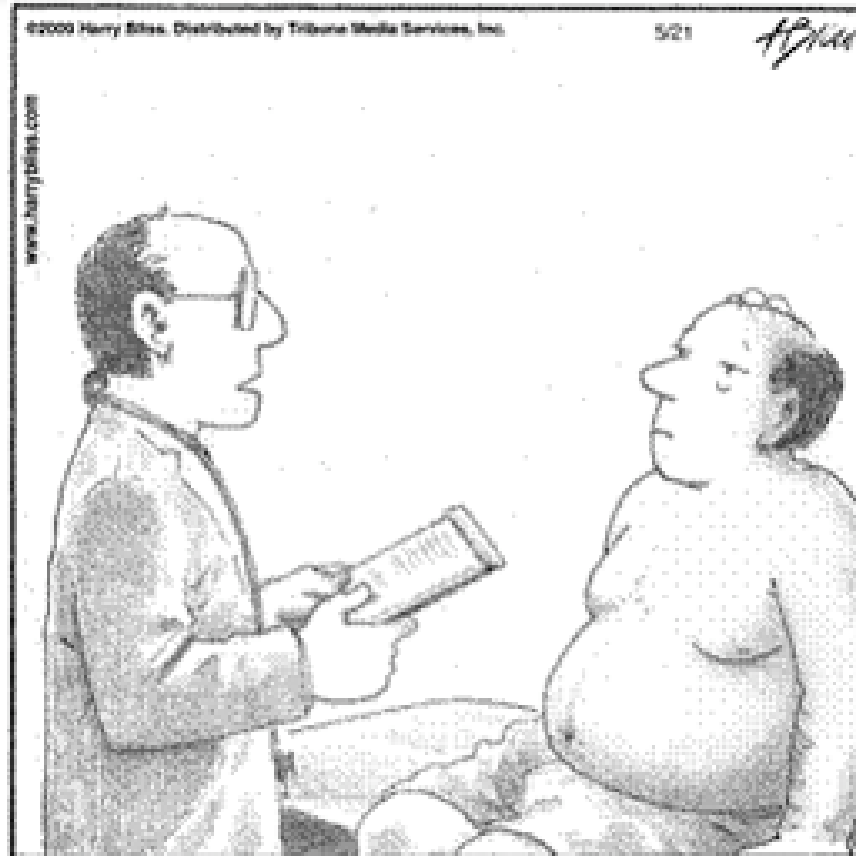
Condition	Product	Indication	Off label use
Sotos syndrome + congenital heart disease + heart failure as a baby	IV furosemide	congestive heart failure and edema	As a baby used IV furosemide orally to reduce fluid load as there was no suitable per os dose
Macular degeneration	Avastin	Renal Cell carcinoma, Non-Small-Cell Lung carc., Breast, Colorectal and Ovarian neoplasms	My father had an injection of Avastin for macular degeneration on 20/02/2012 and the drug was contaminated. He went blind within two hours. I now know 14 patients who were affected by this batch
Narcolepsia cataplexia	teronac	Short-term (i.e., a few weeks) treatment of exogenous obesity (amphetamine like)	1 dose per day, lifelong, with Modiodal and Effexor



Were you comfortable with it being off-label?



	Yes	Somewhat	No
English	54	9	7
French	38	8	4
German	58	17	5
Italian	17	9	2
Spanish	9	7	12
TOTAL	176	50	30



"Well, yes, I suppose I could explain the test results in 'plain English' — but then you'd know how sick you are."