World Health Organization

The classification of medicinal substances

INN and ATC
Proposal of a WHOA Course

57 Meeting of the WHO Advisory Group
for Drug Statistics Methodology
3 April 2025

Discussions and proposals of chemical working group

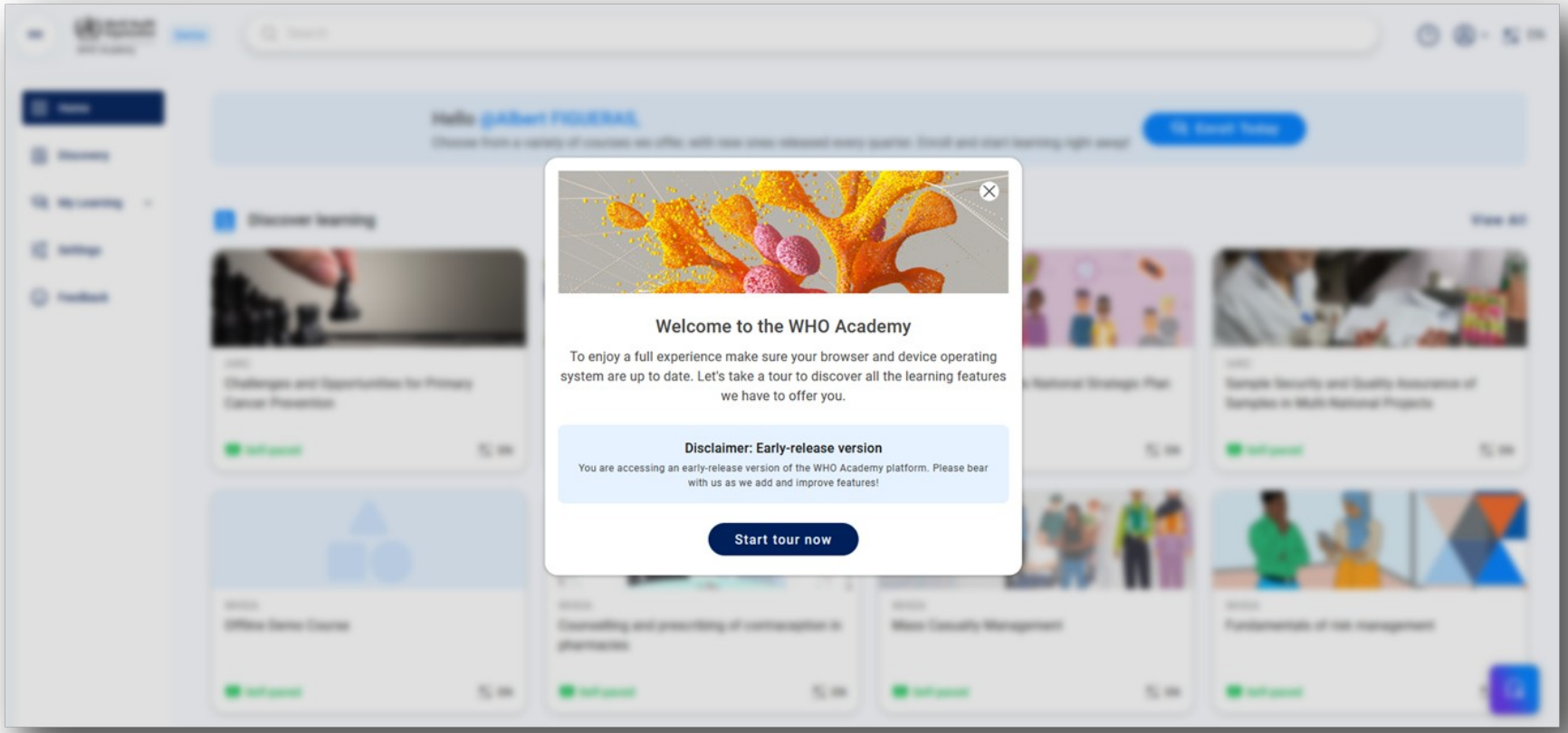
A. Getting structure information in electronic format

B. Unification of representation for oligonucleotides

C. Unification of names and representation for isotopically labeled substances

D. Progress with preparation of files for PL133

the WHO Academy



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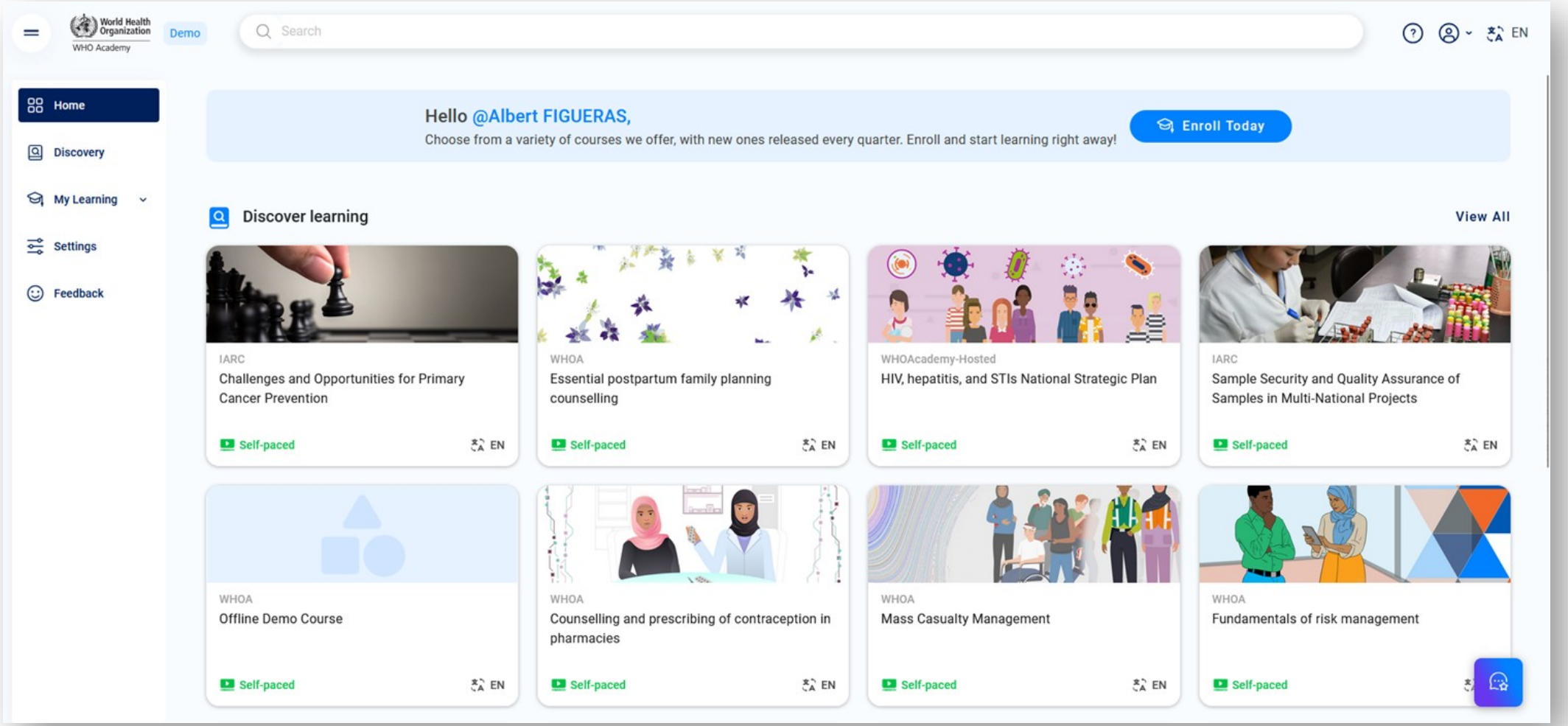
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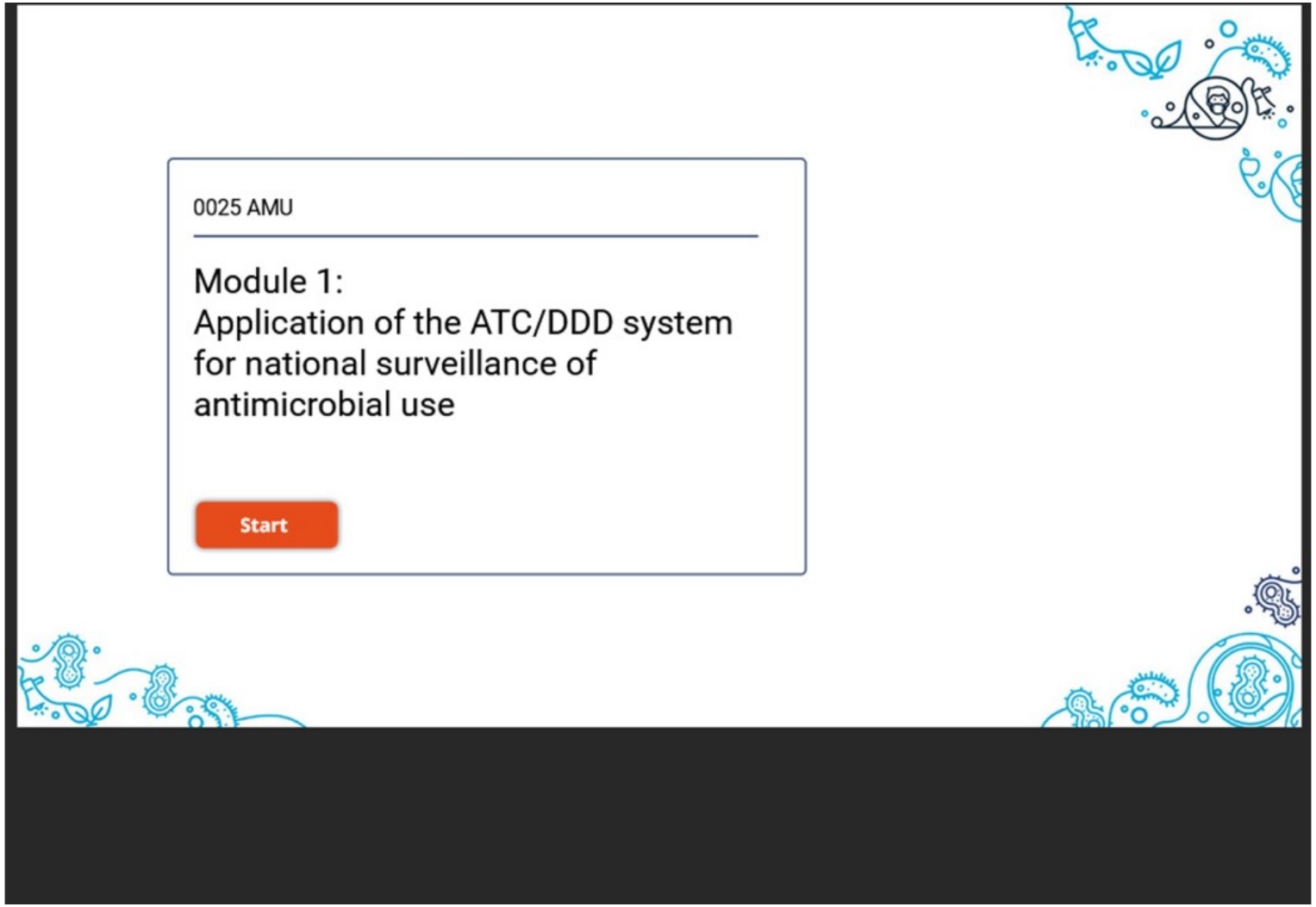
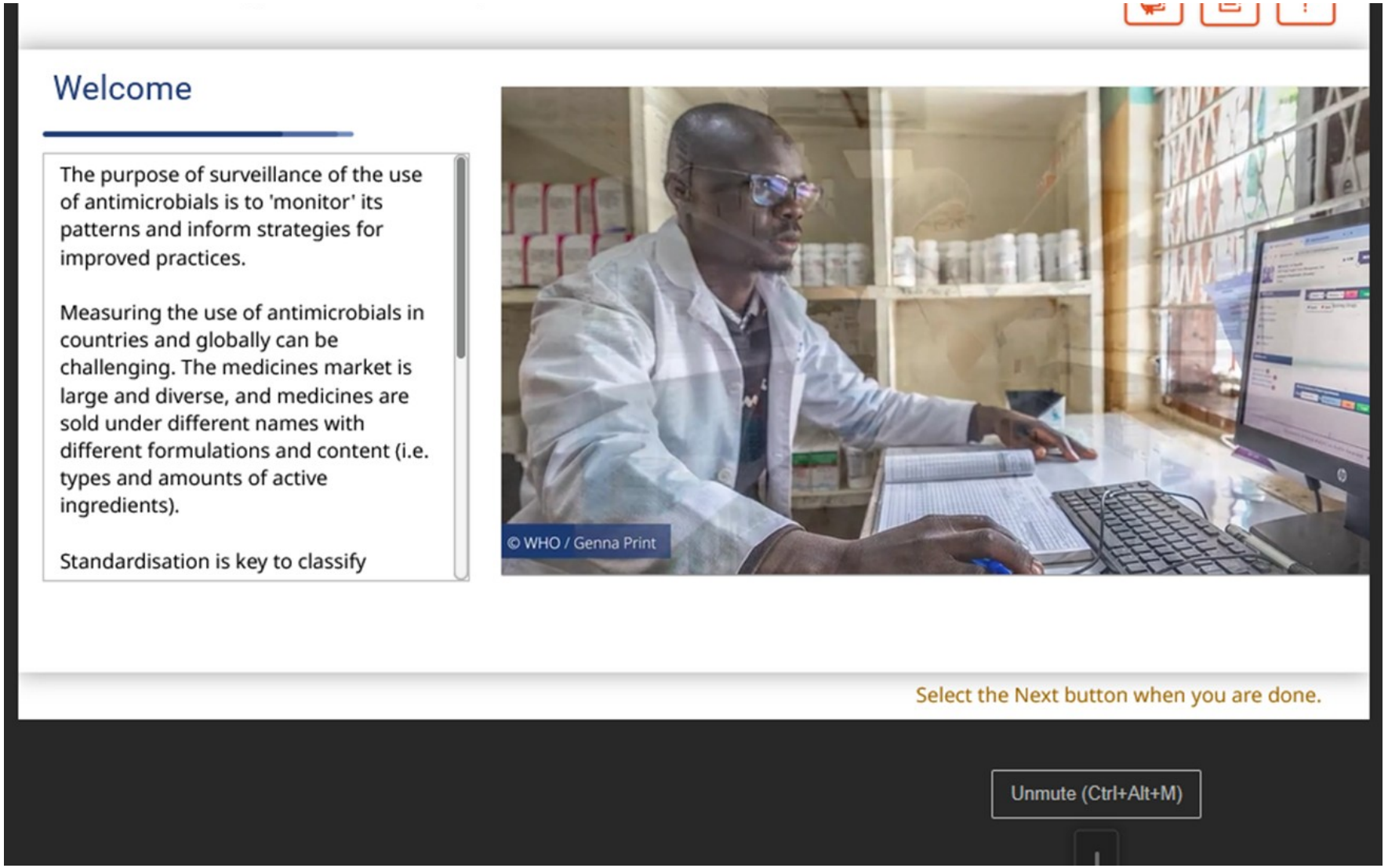
- On-line courses
- Self-paced
- Interactive
- No professor, mentor, external feedback

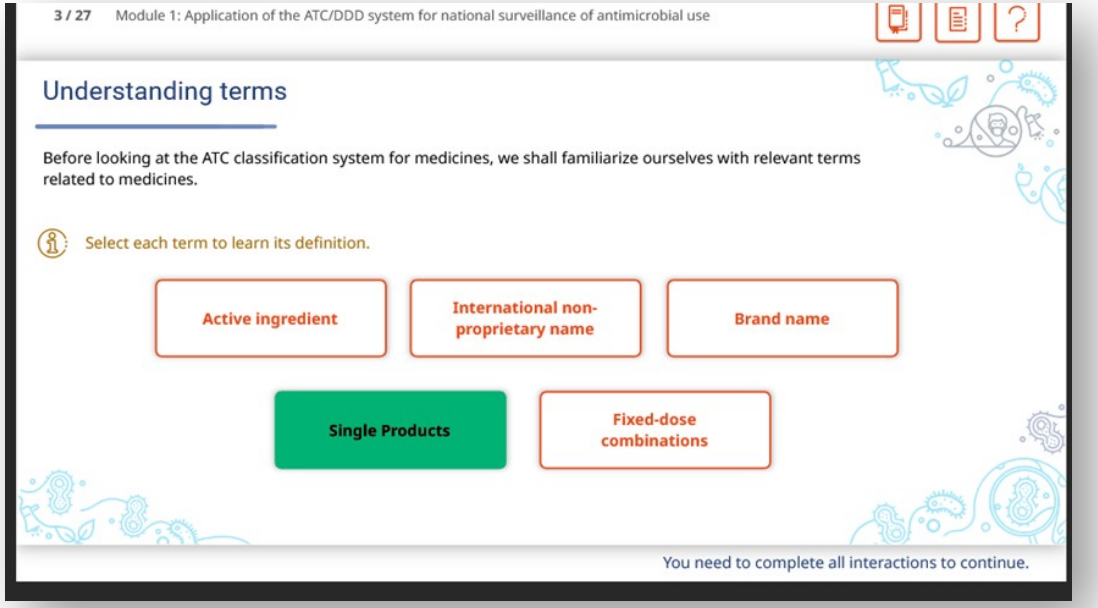
How it looks - An example

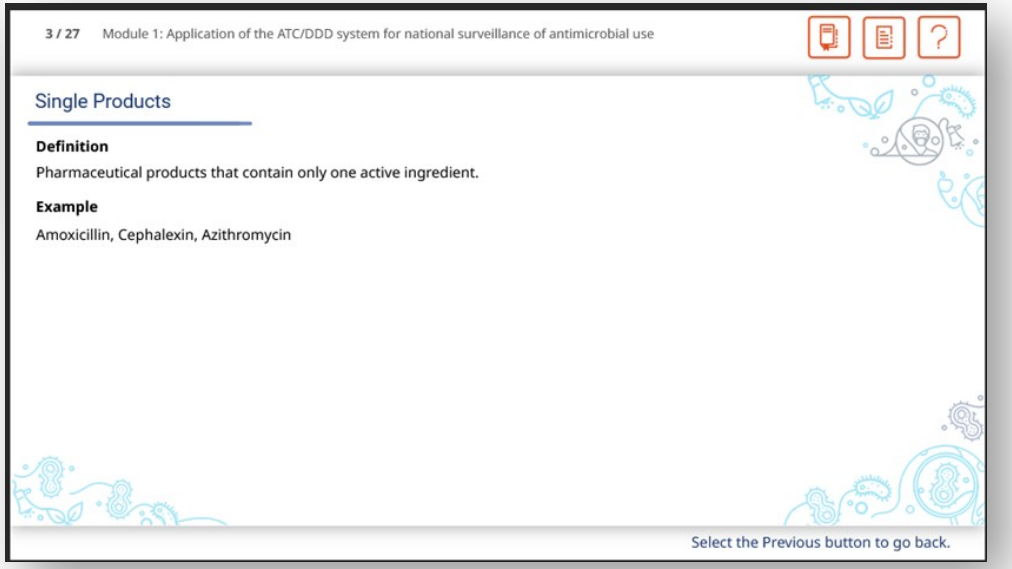


How it looks – Narrated videos

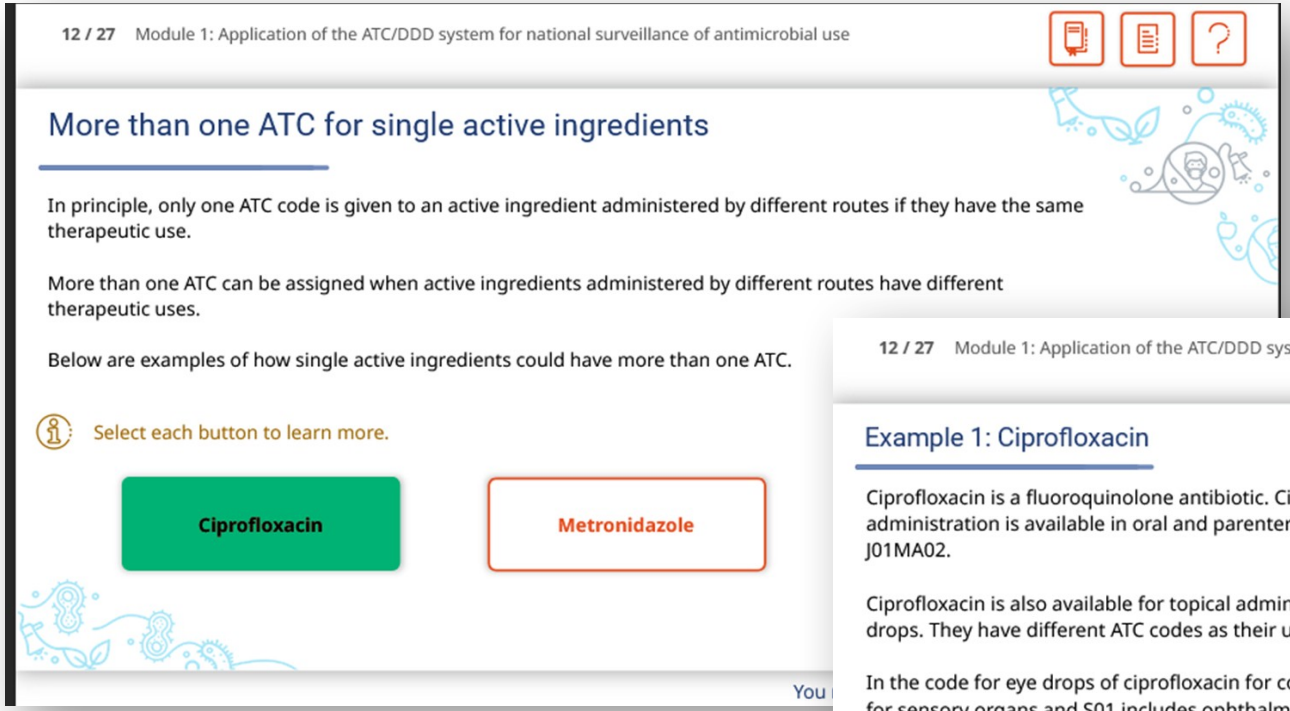


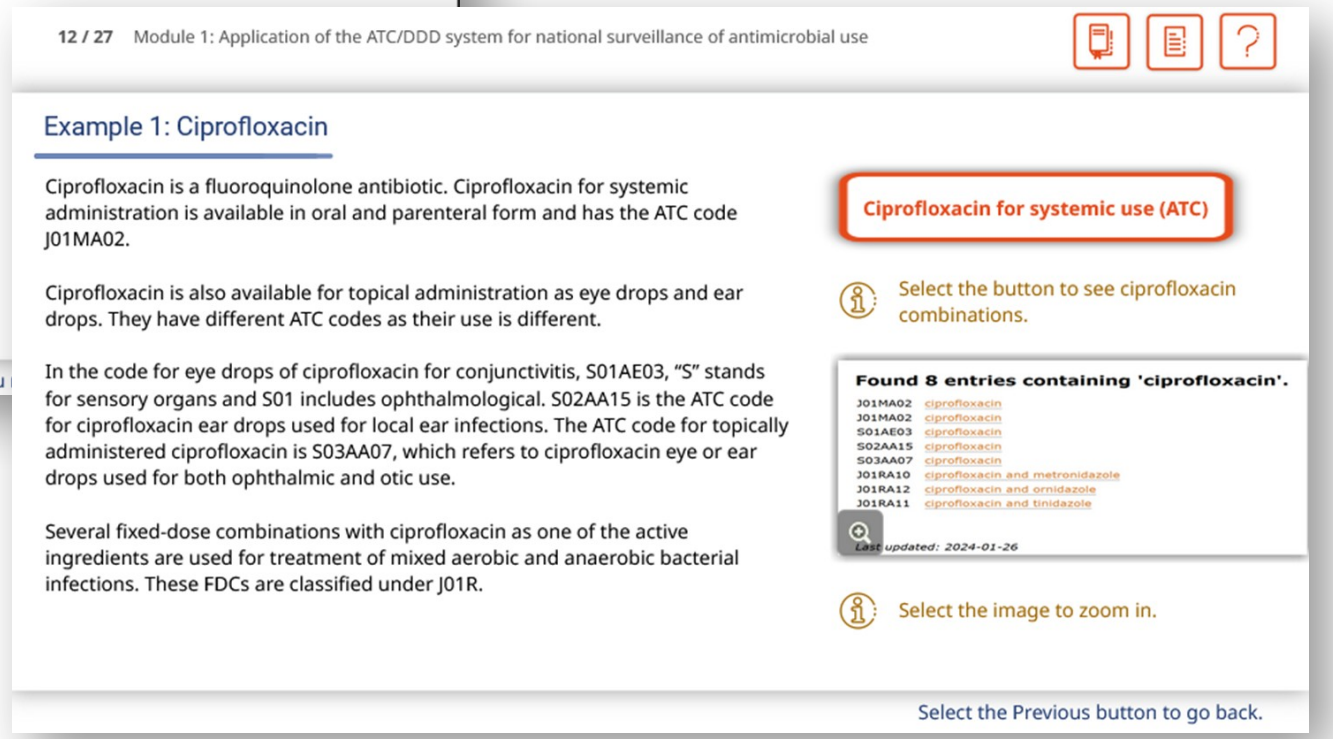
How it looks – explaining concepts (1)



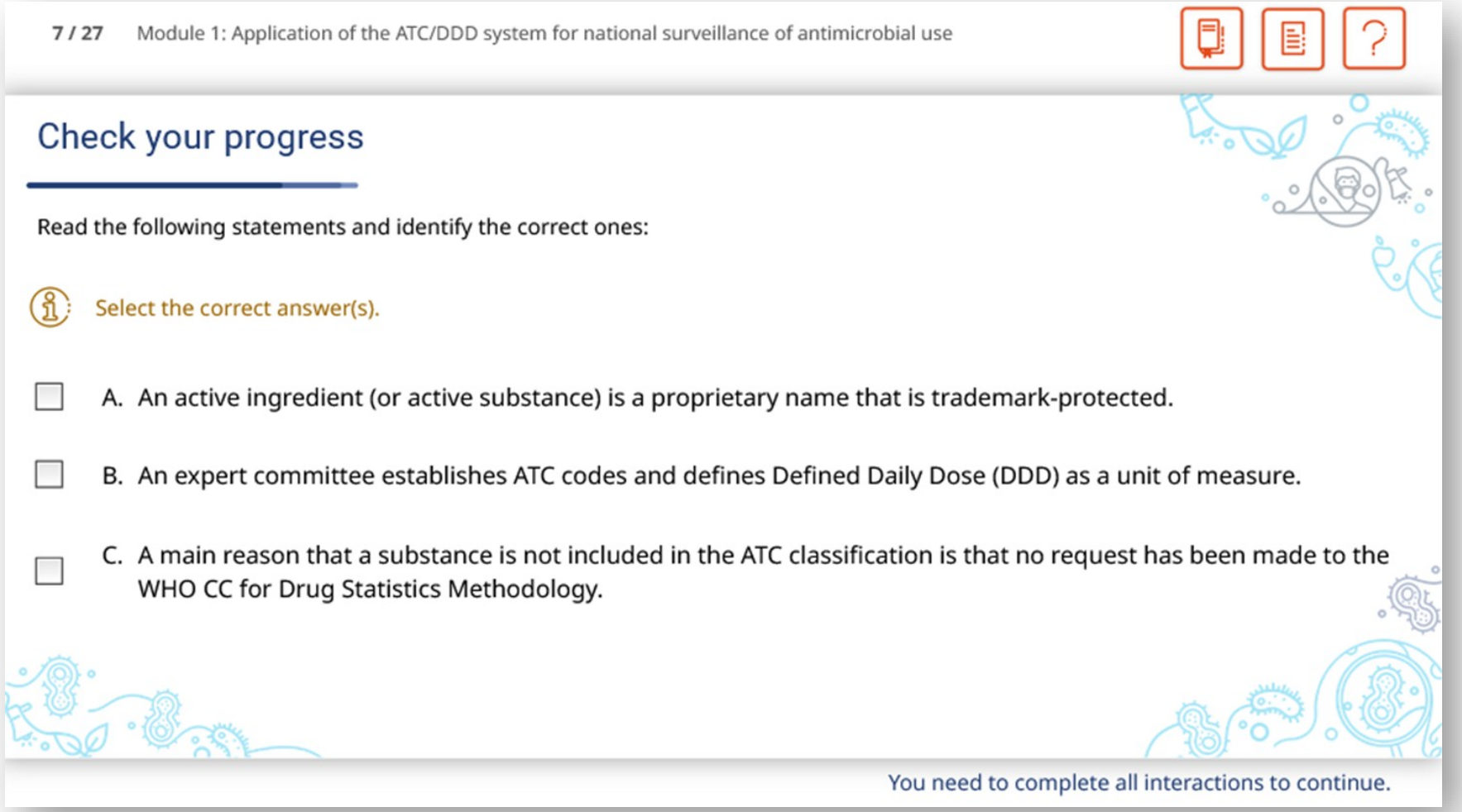


How it looks – explaining concepts (2)

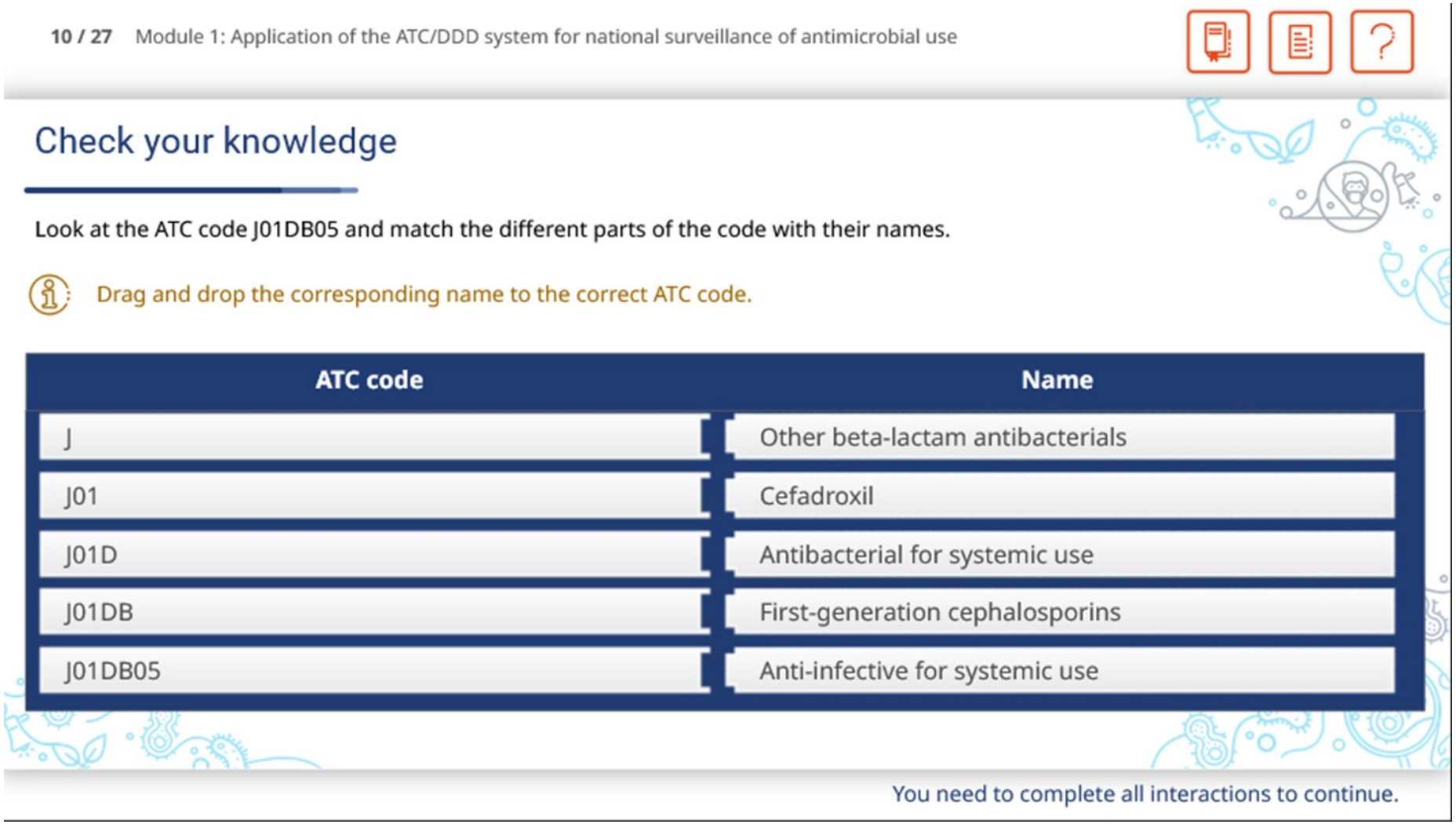




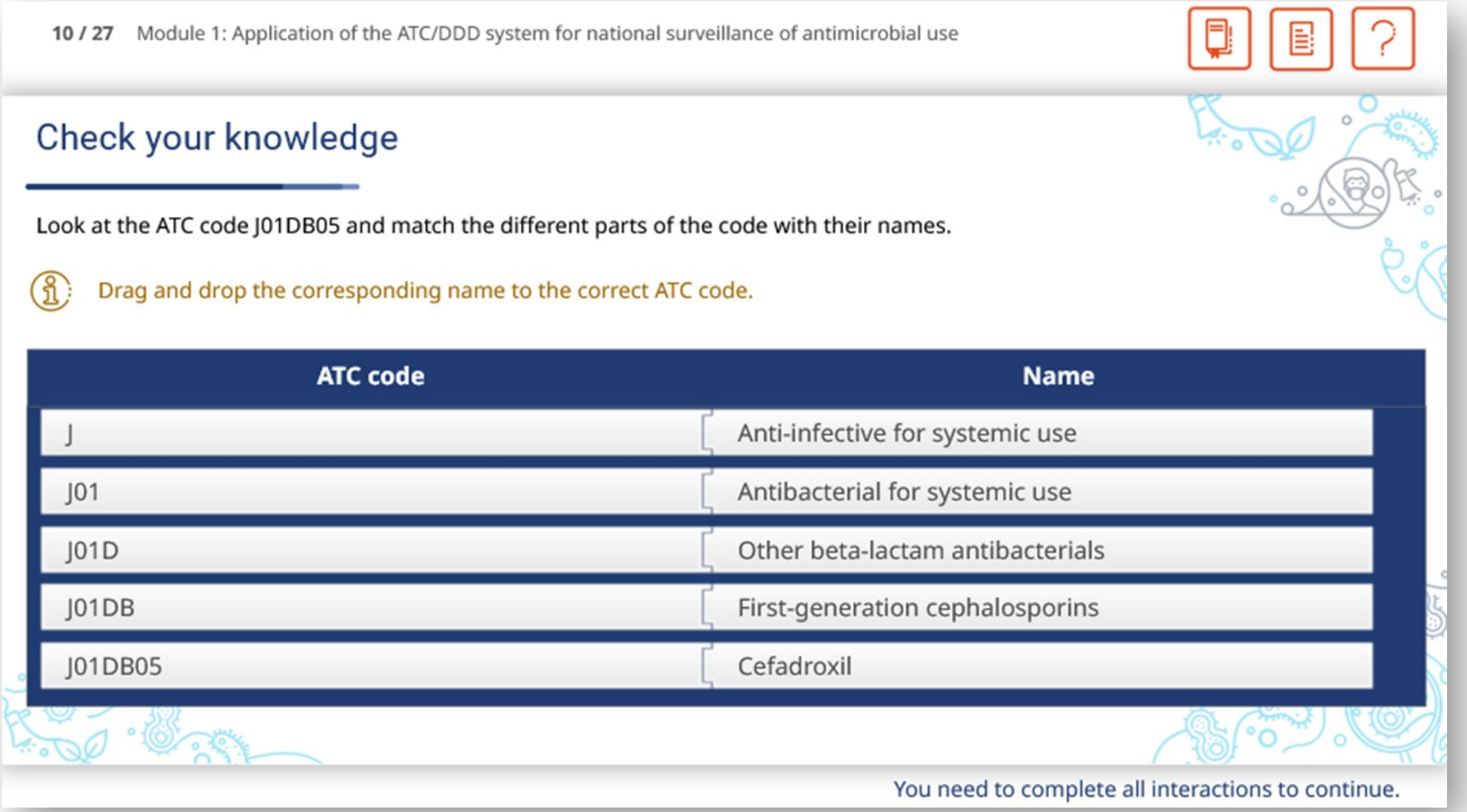
How it looks – exercises, knowledge check



How it looks – exercises, gaming



How it looks – exercises, gaming



Lesson 1.- Introduction

Lesson 2.- Introduction to the INN system - From its foundation to the challenge of naming complex therapies

Lesson 3.1.- The ATC System – Introduction to the classification .principles and use

.**Lesson 3.2.-** The DDD unit – Concept and basic use

Lesson 4.- Comparison and interrelation between the INN and the .ATC/DDD

Lesson 5.- Practical Applications of the ATC/DDD and the INN

WHOA developing process

"DIE HARD"

FADE IN

1 405 FREEWAY - LOS ANGELES - EARLY EVENING 1

Christmas tinsel on the light poles. We ARE LOOKING east past Inglewood INTO the orange grid of L.A. at night when suddenly we TILT UP TO CATCH the huge belly of a landing 747 — the noise is deafening.

2 INT. 747 - PASSENGERS - SAME 2

The usual moment just after landing when you let out that sigh of relief that you've made it in one piece. As the plane TAXIS to its gate, they stir, gather personal belongings.

3 ON JOHN MCCLANE 3

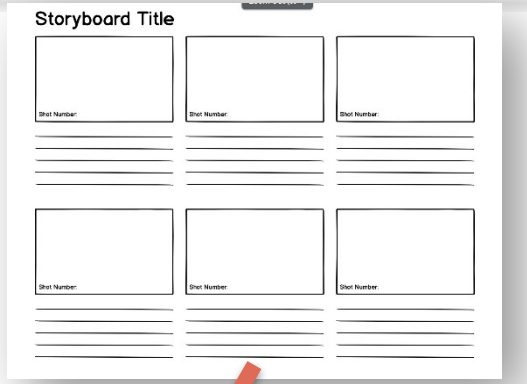
mid-thirties, good-looking, athletic and tired from his trip. He sits by the window. His relief on landing is subtle, but we NOTICE. Suddenly, he hears —

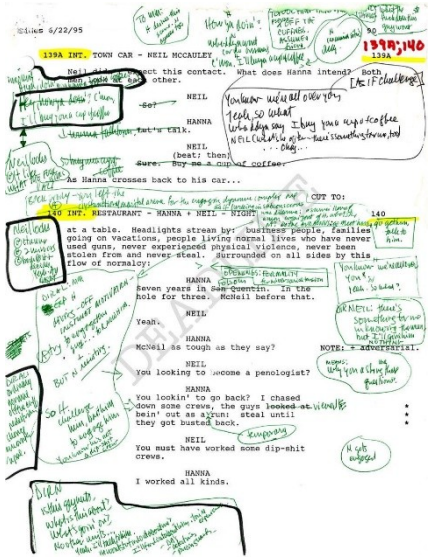
SALESMAN'S VOICE
You don't like flying, do you?

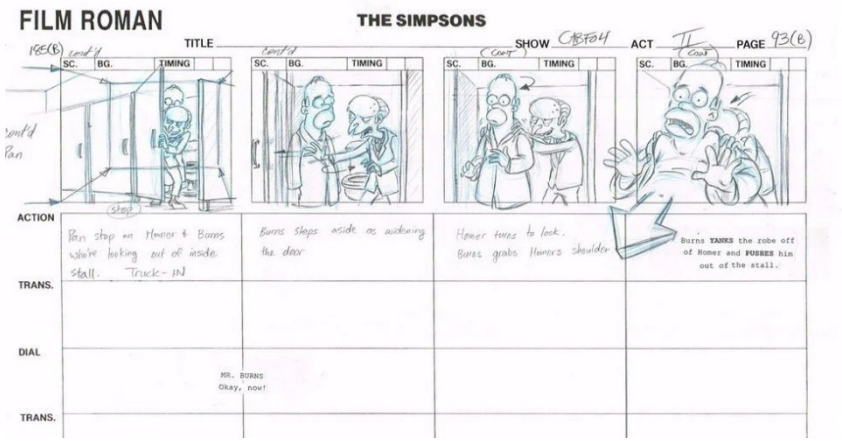
McClane turns, looks at the Babbit clone next to him. Caught, he tenses, holds his armrests in exaggerated fear.

MCCLANE
No, no, where'd you get that idea?

SALESMAN
(smiling)
Ya wanna know the secret of successful air travel? After you get where you're going, ya take off your shoes and socks. Then ya walk around on the rug barefoot and make fists with your toes.







INN-ATC course – Examples of scenarios, activities and interaction

Scenario 1:

But who are these mysterious wordsmiths, seemingly playing linguistic puzzles while crafting medicine names?

[ANIMATED VIDEO WITH VOICE AND CHARACTERS]

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Three medical residents – Sarah (oncology), Mike (respiratory), and Elena (rheumatology) – meet for coffee after a long week of rotations.

Sarah: So today, I had to present a new breast cancer medicine in rounds. I tried three times before I could say 'datopotamab deruxtecan' without stumbling.

Robert: Oh, come on, that's nothing! Try announcing 'benralizumab' in front of the whole department while sleep-deprived. Called it 'ben-rala-something' and my student just smirked.

Elena: At least yours sound somewhat pronounceable. Yesterday I had to explain to a patient about entering a clinical trial of 'tafasitamab vedotin'. The patient just stared at me and said 'Can't you just write that down?'.

Robert: "What's with all these 'mabs' anyway? It seems like every new medicine ends in 'mab' these days.

Sarah: Ah, that is because they are monoclonal antibodies. But wait until you see what is coming. Now we have got 'barts' and 'tafusps' and...

Elena: Seriously? Who comes up with these names? It's like they are playing some twisted version of Scrabble!

Robert: "Hey, at least we're not in dermatology. My friend there has to deal with creams combining three of these unpronounceable names in one product.

Sarah: (showing her phone) Look at this one I'm supposed to present next week... 'tebentafusp'. My tongue will have cramps.

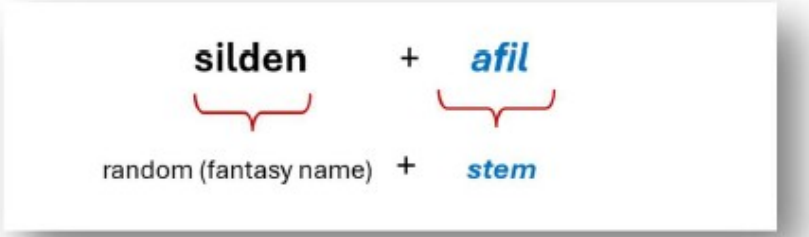
Elena: You know what is funny? We will probably complain that these were the simple names in twenty years. I can see us, already chiefs of the department saying: 'Back in my day, drugs only had four syllables...'

[SCENARIO 1 ENDS]

2.2. INN system schemes

[ANIMATED VIDEO WITH VOICE]

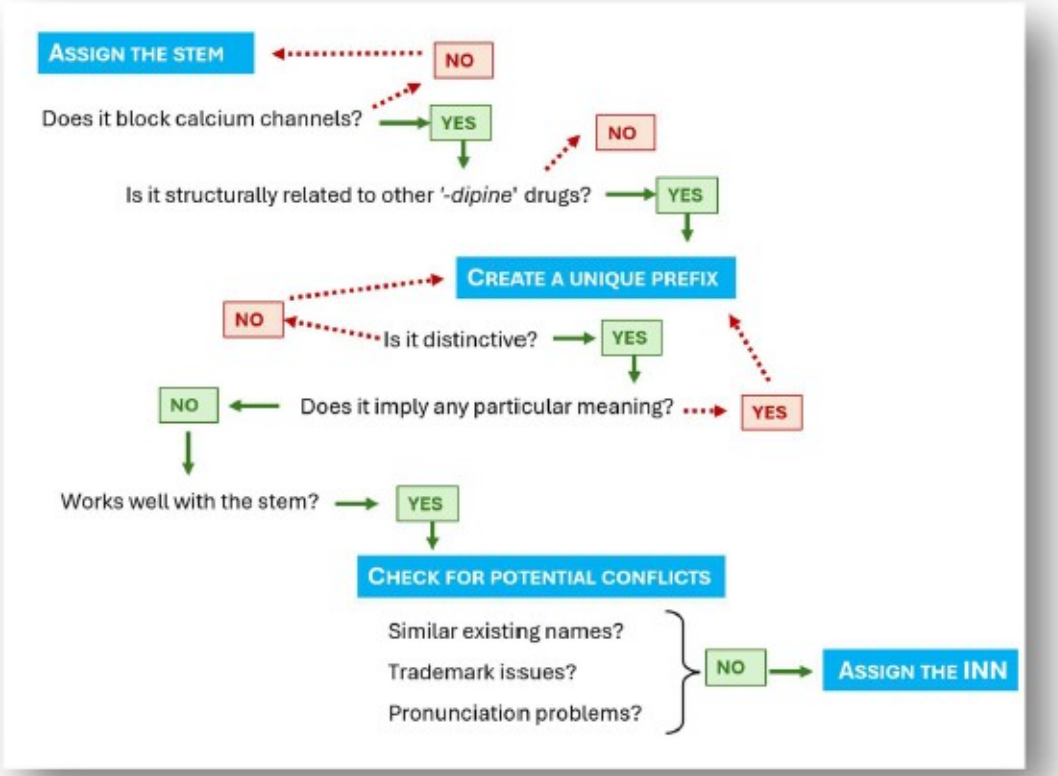
Usually, an INN consists of a random (fantasy) prefix and a common stem. Substances belonging to a group of pharmacologically related substances show their relationship using a common suffix called "stem".
For example, the structure of the INN "sildenafil" is:



The stem is "*-afil*", described as "inhibitors of phosphodiesterase PDE5 with vasodilator action". Therefore, other substances sharing the same mechanism of action will be named as:

Sometimes, the random prefix + stem scheme is increased with an infix or "sub-stem", established to differentiate between different related groups of substances.

[ANIMATED SCREENS WITH VOICE]



[VOICE]

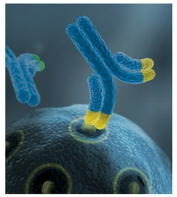
First, it is necessary to confirm that the stem applies using the available information. Remember that, at this stage, applications are for substances in the initial stages of clinical development, and the available data is scarce.

If your answer to both questions is "Yes", the stem is correct, and you can proceed to the creation of a prefix (random prefix). If it is a distinctive name and it does not imply any particular meaning, then you should check for possible conflicts.

3.1. Evolution of monoclonal antibodies naming

[SLIDES WITH VOICE]

A "monoclonal antibody" is an antibody produced from a cell lineage made by cloning a unique white blood cell. Currently, they are used in diagnosing illnesses such as cancer and infections and treating cancer and inflammatory diseases, among other conditions.



The first licenced monoclonal antibody was muromonab-CD3, approved in 1986 to prevent kidney transplant rejection. Since then, monoclonal antibodies have revolutionised medicine but naming them has become increasingly complex.

Originally, all antibody-based drugs ended with "-*mab*" (like adalimumab or rituximab), making them easily recognisable by doctors and pharmacists.

Old system

rituximab

ri- **tu-** + **-xi-** + **-mab**

- **-mab**: monoclonal antibody stem
- **-xi-**: chimeric source
- **tu-**: targeting tumours
- **ri-**: random prefix

General principles of the ATC codes

The following animation will show what an ATC code looks like.

[ANIMATION STARTS]

Let's start with an example.

Haloperidol is a medicine used in the treatment of certain psychoses.

Its ATC code is "N05AD01"

haloperidol	N05AD01

haloperidol	N05AD01
diclofenac	M01AB05
propranolol	C07AA05
trastuzumab	L01FD01

All ATC codes are a combination of letters and numbers. For example, the ATC code for *diclofenac* is "M01AB05", while "C07AA05" corresponds to propranolol and "L01FD01" to trastuzumab.

However, these letters and numbers are not assigned randomly.

Step-by-step demonstration

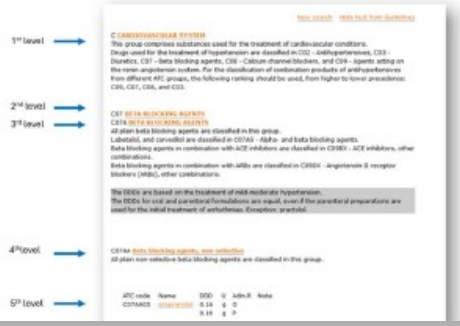
1. Open the ATC/DDD webpage in your browser

2. Write the name of the substance you are looking for. In this case, “propranolol”.

Please note that the webpage only admits names in English. Otherwise, it will not retrieve any results.

3. Click the *Search* button.

4. The new screen shows different entries. Let’s click on the first one.



5. The webpage will automatically open a new screen, where you can identify the ATC code (C07AA05), and also the different levels, starting for the main anatomical group (Cardiovascular system).

centres in the last quarter to start the procurement admin for the next quarter. Therefore, John asked the pharmacists of each centre for the list containing the number of supplied boxes, vials and bottles for each medicine used. Once he has the complete list, John starts with the first one: alprazolam. His screen shows the following table:

Primary Healthcare Centre	Product	Number packages
1	Alprazolam_AAA, 12 tablets, 2 mg	132
2	Alprazolam_DDD, 30 tablets, 0.5 mg	256
3	Alprazolam_AAA, 18 tablets, 1 mg	78
4	Alprazolam_AAA, 025mg/ml, bottle 60 ml	86
5	Alprazo	

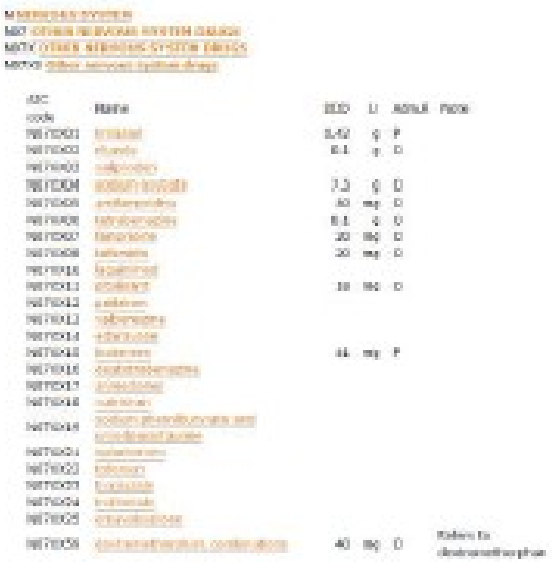
[SOLUTION]

This is the final table. The total number of DDD sold are 167.65:

Product	Content x unit (g)	Nr units x package	g per package	ATC code	DDD value (g)	DDD per package	Nr packages sold	Total Nr DDDs sold
Metronidazole_AAA, 15 tablets, 0.4 g	0.4	15	6	P01AB01	2 g	3	32	96
Metronidazole_AAA, 28 tablets, 0.2 g	0.2	28	5.6	P01AB01	2 g	2.8	25	70
Metronidazole_PPP, 0.5 g, flacon 100 mL	0.5	1	0.5	J01XD01	1.5 g	0.33	5	1.65
TOTAL							62	167.65

[NOW YOU TRY IT]

Below, there is another example. It includes a few medicines classified in the N07XX subgroup, belonging to the nervous system drugs (N), under Other nervous system drugs (N07).



This subgroup lists 24 drugs; we will examine only eight of them.

Now, look at the table including the INN, stem definitions and intended use of this heterogeneous group of

ATC code	INN	stem definition	intended use
N07XX10	laquinimod	-imod immunomodulators, both stimulant/suppressive and stimulant	multiple sclerosis / Huntington's disease
N07XX11	pitolisant	-isant histamine H3 receptor antagonists and inverse agonists	narcolepsy
N07XX12	patisiran	-siran small interfering RNA including siRNA, miRNA and piRNA	polyneuropathy in people with hereditary transthyretin-mediated amyloidosis
N07XX15	inotersen	-rsen antisense oligonucleotides	treatment of nerve damage in adults with hereditary transthyretin-mediated amyloidosis
N07XX18	vutrisiran	-siran small interfering RNA including siRNA, miRNA and piRNA	polyneuropathy in people with hereditary transthyretin-mediated amyloidosis
N07XX21	eplontersen	-rsen antisense oligonucleotides	treatment of transthyretin-mediated amyloidosis
N07XX22	tofersen	-rsen antisense oligonucleotides	amyotrophic lateral sclerosis
N07XX24	trofinetide	-tide peptides and glycopeptides; -netide neurological	treatment of Rett syndrome

substances sharing the same ATC chemical subgroup.

Now, pair the mechanisms of action included in the next table with the name of the active ingredients of the previous table:

List of INNs: trofinetide; tofersen; eplontersen; vutrisiran; inotersen; patisiran; pitolisant; laquinimod

mechanism of action	INNs
immunomodulator	
histamine H3 receptor antagonist	
small interfering RNA	
antisense oligonucleotide	
neurological peptides	

Go to pr

[FEEDBACK]

mechanism of action	INNs
immunomodulator	laquinimod
histamine H3 receptor antagonist	pitolisant;
small interfering RNA	patisiran; vutrisiran
antisense oligonucleotide	inotersen; eplontersen; tofersen
neurological peptides	trofinetide

Scenario 2:

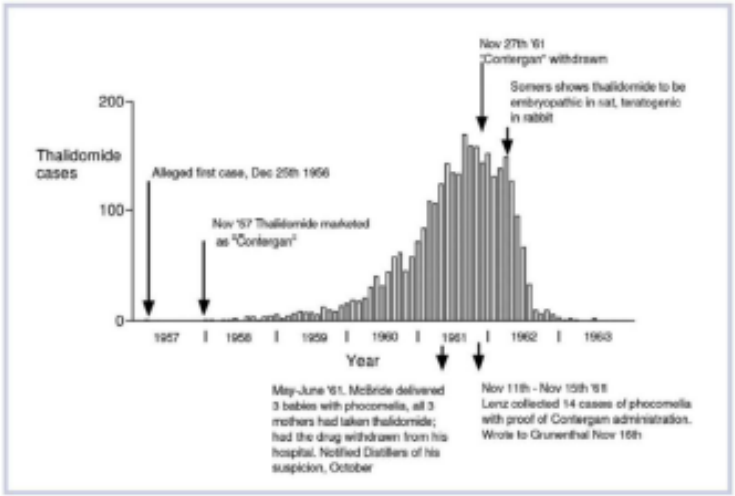
Using the INN stems in pharmacovigilance: research on the safety profile and aid in early signal detection

Background information - Pharmacovigilance

[VIDEO WITH VOICE]

Pharmacovigilance involves the surveillance and study of adverse drug reactions and the early detection of any unexpected or previously unknown harm associated with medicines.

Pharmacovigilance has been developed to detect any signal of potential harm, especially of new medicines as soon as possible and, therefore, try to prevent disasters that affected many patients before the discovery of the iatrogenic causality. One of the best known of such disasters is the epidemic of phocomelia, a rare congenital malformation associated with the use of thalidomide by pregnant women in the early 1960s. By the time the causal relationship was established, three years after the first cases, more than 10,000 babies were affected by this serious adverse drug reaction.



[EXERCISE]

The following screens show the results of the VigiAccess search for canagliflozin and dapagliflozin.

canagliflozin

Reported potential side effects

- Blood and lymphatic system disorders (0%, 133 ADRs)
- Cardiac disorders (2%, 803 ADRs)
- Congenital, familial and genetic disorders (0%, 40 ADRs)
- Ear and labyrinth disorders (0%, 88 ADRs)
- Endocrine disorders (0%, 34 ADRs)
- Eye disorders (1%, 310 ADRs)
- Gastrointestinal disorders (5%, 2 301 ADRs)
- General disorders and administration site conditions (8%, 3 665 ADRs)
- Hepatobiliary disorders (0%, 159 ADRs)
- Immune system disorders (1%, 250 ADRs)
- Infections and infestations (16%, 7 050 ADRs)
- Injury, poisoning and procedural complications (6%, 2 462 ADRs)
- Investigations (8%, 3 647 ADRs)
- Metabolism and nutrition disorders (13%, 5 816 ADRs)
- Musculoskeletal and connective tissue disorders (2%, 1 061 ADRs)
- Neoplasms benign, malignant and unspecified (incl cysts and polyps) (1%, 231 ADR
- Nervous system disorders (5%, 2 229 ADRs)
- Pregnancy, puerperium and perinatal conditions (0%, 19 ADRs)
- Product issues (0%, 120 ADRs)
- Psychiatric disorders (1%, 595 ADRs)
- Renal and urinary disorders (9%, 4 128 ADRs)
- Reproductive system and breast disorders (2%, 668 ADRs)
- Respiratory, thoracic and mediastinal disorders (1%, 560 ADRs)
- Skin and subcutaneous tissue disorders (7%, 2 868 ADRs)
- Social circumstances (0%, 95 ADRs)
- Surgical and medical procedures (8%, 3 615 ADRs)
- Vascular disorders (2%, 845 ADRs)

dapagliflozin

Reported potential side effects

- Blood and lymphatic system disorders (0%, 323 ADRs)
- Cardiac disorders (3%, 1 955 ADRs)
- Congenital, familial and genetic disorders (0%, 137 ADRs)
- Ear and labyrinth disorders (1%, 360 ADRs)
- Endocrine disorders (0%, 102 ADRs)
- Eye disorders (1%, 870 ADRs)
- Gastrointestinal disorders (7%, 4 756 ADRs)
- General disorders and administration site conditions (14%, 9 302 ADRs)
- Hepatobiliary disorders (1%, 336 ADRs)
- Immune system disorders (1%, 372 ADRs)
- Infections and infestations (13%, 8 450 ADRs)
- Injury, poisoning and procedural complications (4%, 2 903 ADRs)
- Investigations (9%, 6 196 ADRs)
- Metabolism and nutrition disorders (10%, 6 644 ADRs)
- Musculoskeletal and connective tissue disorders (3%, 1 874 ADRs)
- Neoplasms benign, malignant and unspecified (incl cysts and polyps) (1%, 695 ADRs)
- Nervous system disorders (7%, 4 346 ADRs)
- Pregnancy, puerperium and perinatal conditions (0%, 8 ADRs)
- Product issues (0%, 299 ADRs)
- Psychiatric disorders (2%, 1 292 ADRs)
- Renal and urinary disorders (8%, 5 049 ADRs)
- Reproductive system and breast disorders (4%, 2 579 ADRs)
- Respiratory, thoracic and mediastinal disorders (2%, 1 465 ADRs)
- Skin and subcutaneous tissue disorders (6%, 3 740 ADRs)
- Social circumstances (0%, 212 ADRs)
- Surgical and medical procedures (1%, 345 ADRs)
- Vascular disorders (2%, 1 250 ADRs)

Identify the three most frequently reported ADR systems (in %) for both drugs:

Position	Canagliflozin	Dapagliflozin
1		
2		
3		

[FEEDBACK]

Position	Canagliflozin (% of ADRs)	Dapagliflozin
1	Infections and infestations (16%)	General disorders and administration site conditions (14%)
2	Metabolism and nutrition disorders (13%)	Infections and infestation (13%)
3	Renal and urinary disorders (9%)	Metabolism and nutrition disorders (10%)