Search and Analysis of Chemical Formulations – From Recipes to Complex Dosage Forms

Maik Annies
Syngenta AG, Switzerland

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Agenda

- **Introduction**
  - What are chemical formulations?
  - Recipes and formulation types/dosage forms
  - Why are formulations important in business and IP?
- **Best practice in formulation searching and analysis**
  - Patent literature
  - Non-patent literature
  - The Internet

What are chemical formulations?

Combinations of active ingredients and inert formulation components, which are more effective than the active ingredients alone

Agrochemistry

Pharmaceuticals

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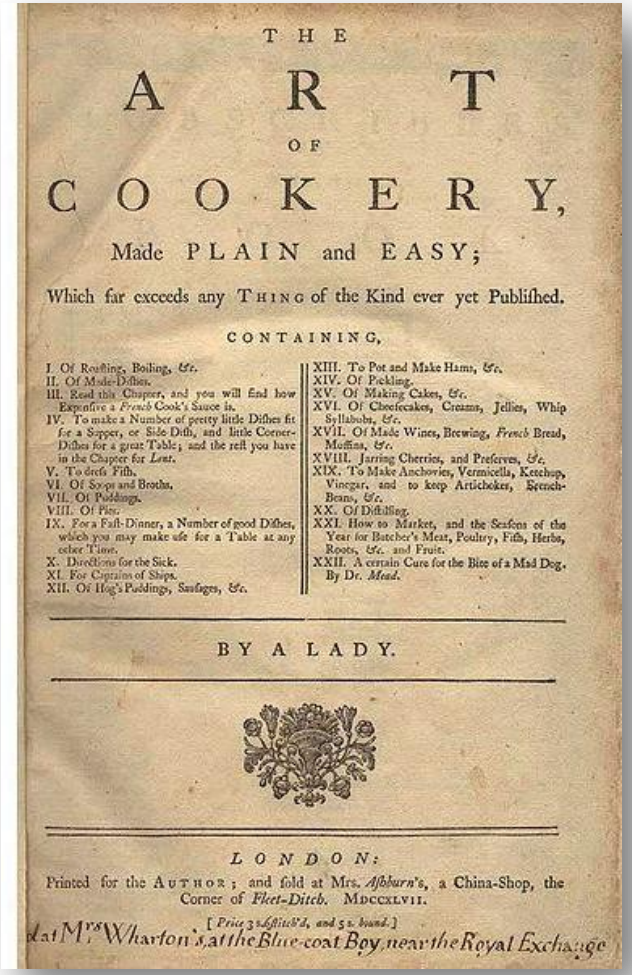
Formulation recipes

- **Formulation recipes** define the exact composition of active ingredients and formulation components
- **Active ingredients (AI)** are chemical compounds with a biological activity, e.g. pharmaceuticals, agrochemicals (pesticides, fertilizers), etc.
- **Formulation components** are inert chemical compounds improving the properties of active ingredients with regards to effectiveness, application, safety or storage



THE

ART

OF

COOKERY,

Made PLAIN and EASY;

Which far exceeds any THING of the Kind ever yet Publiſhed.

CONTAINING,

I. Of Roaſting, Boiling, &c.
II. Of Made-Diſhes.
III. Read this Chapter, and you will find how Expenſive a *French* Cook's Sauce is.
IV. To make a Number of pretty little Diſhes fit for a Supper, or Side Diſh, and little Corner-Diſhes for a great Table; and the reſt you have in the Chapter for *Lent*.
V. To dreſs Fiſh.
VI. Of Soops and Broths.
VII. Of Puddings.
VIII. Of Pies.
IX. For a Full-Dinner, a Number of good Diſhes, which you may make uſe for a Table at any other Time.
X. Directions for the Sick.
XI. For Captains of Ships.
XII. Of Hog's Puddings, Sauſages, &c.
XIII. To Pot and Make Hams, &c.
XIV. Of Pickling.
XV. Of Making Cakes, &c.
XVI. Of Cheeſecakes, Creams, Jellies, Whip Syllabubs, &c.
XVII. Of Made Wines, Brewing, *French* Bread, Muffins, &c.
XVIII. Jarring Cherries, and Preſerves, &c.
XIX. To Make Anchovies, Vermicella, Ketchup, Vinegar, and to keep Artichokes, French-Beans, &c.
XX. Of Diſtilling.
XXI. How to Market, and the Seaſons of the Year for Butcher's Meat, Poultry, Fiſh, Herbs, Roots, &c. and Fruits.
XXII. A certain Cure for the Bite of a Mad Dog. By Dr. *Mead*.

BY A LADY.

LONDON:

Printed for the AUTHOR; and ſold at Mrs. *Aſhburn*'s, a China-Shop, the Corner of *Fleet-Ditch*. MDCCXLVII.

[*Price* 3 *s. ſtitch'd, and* 5 *s. bound.*]

And at Mrs. Wharton's, at the Blue-coat Boy, near the Royal Exchange

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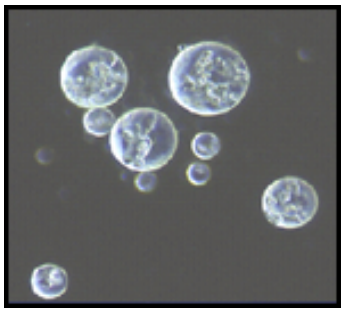
Formulation types and dosage forms

- **Physical form** of chemical formulations as applied to their substrate (patient, plant, etc.)
  - **Examples** of dosage forms and formulation types:
    - **Pharmaceuticals**: pills, capsules, creams, gels, aerosols, etc.
    - **Agrochemistry**: soluble concentrates, suspension concentrates, water-dispersible granules, micro-capsules, etc.



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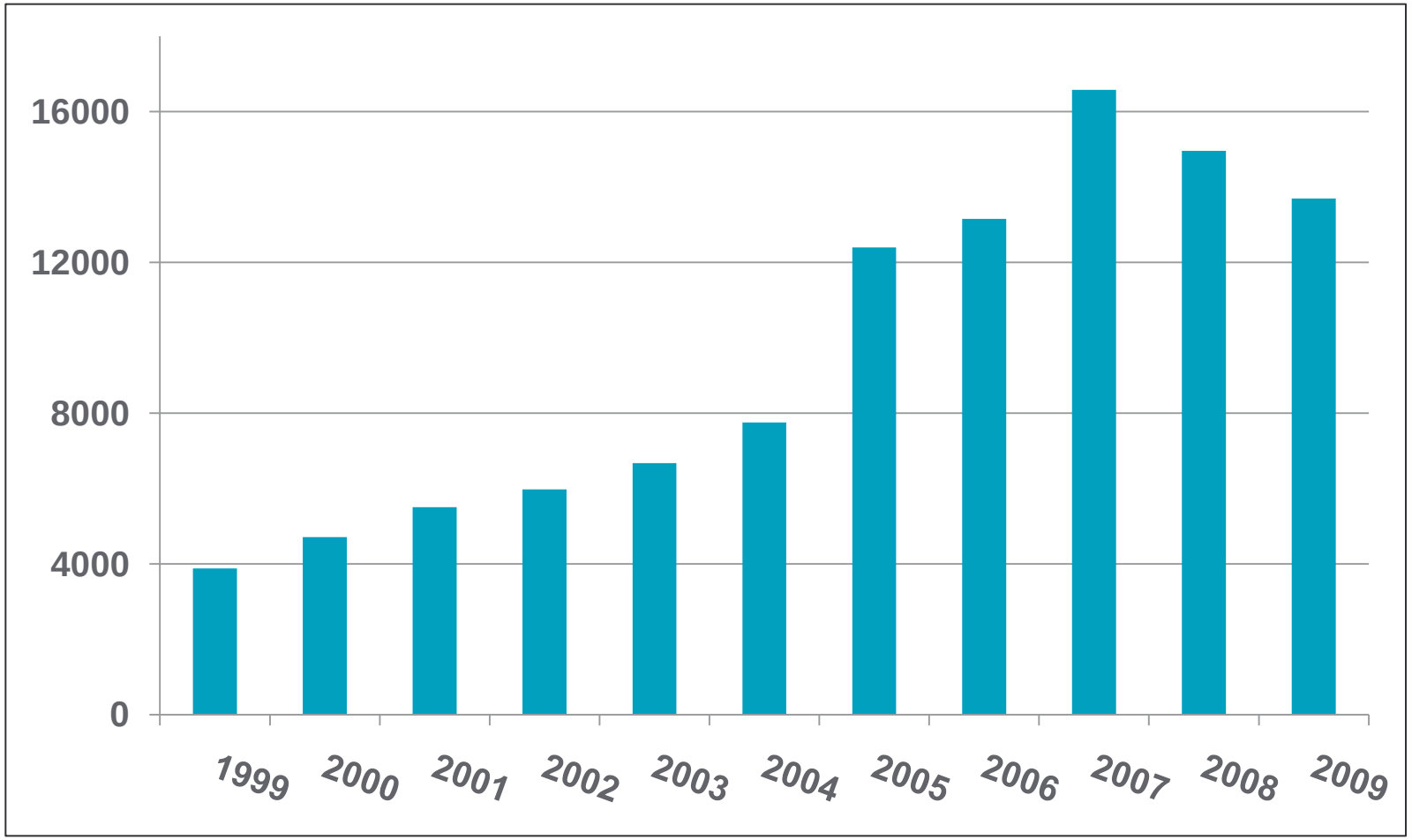
Formulation priority applications per year in agrochemistry and pharmaceuticals in Wold Patents Index



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Why are formulations important in business and IP

- Formulation technology improves properties of active ingredients and therefore makes them fit for purpose
- Active ingredients are normally brought to market not in their pure form but as formulations: formulations are products as sold
- Well represented in chemical companies' product pipelines
- High commercial and patent value

Search and analysis of chemical formulations are highly business critical, since they build the basis for effective reinforcement of patent protection, avoidance of infringement, and competitive analysis

Formulation recipes and how they are claimed

1. An aqueous herbicidal composition comprising:

WO10023198

- an aminophosphate or aminophosphinate salt,
- a surfactant, and
- an organic solvent comprising an N-alkylpyrrolidone wherein the alkyl group comprises at least 2 carbon atoms.

8. A composition according to one of claims 1 to 6, comprising:

- at least 500 g/L of glyphosate potassium salt,
- from 100 to 160 g/L, preferably from 120 to 150 g/L of the amine oxide surfactant, and
- from 1 to 50 g/L of the solvent, preferably from 5 g/L to 25 g/L of the solvent, preferably from 6 g/L to 14 g/L of the solvent, for example from 6 to less than 10 g/L or from 10 to less than 14 g/L.

- Formulation recipes are typically claimed from “generic“ to “specific”
- Both specific and generic aspects of AI, formulation components and their combinations need to be covered by search strategies

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How to search formulation recipes – what should be covered

- Driven by patent law the search should cover e.g.
  - combination(s) of active ingredients
  - combination(s) of active ingredients with each formulation component
  - combination(s) of formulation components
  - general uses of formulation components

Many formulation components and their combinations are standard and already commonly used!

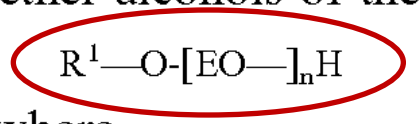
How to search formulation recipes – generic retrieval

- For generic retrieval of active ingredients and formulation components consider
  - Generic chemical names
  - Database codes, controlled vocabulary and patent classifications
  - Derwent Chemical Coding (BCE-coding) and substructure searching in REGISTRY, MARPAT and MMS

How to search formulation recipes – generic retrieval of polymers

15. A solution of organic compounds which are insoluble or insufficiently soluble in lipophilic and hydrophilic media in ether alcohols of the general formula (I)

US20060099157



$$R^1—O-[EO—]_nH \qquad (I)$$

where

R^1 is C_{1-3}-alkyl,

n is on average 7 to 15,

EO is building blocks derived from ethylene oxide.

In case polymers are used as formulation components consider generic polymer searching/coding (e.g. in REGISTRY or World Patents Index)

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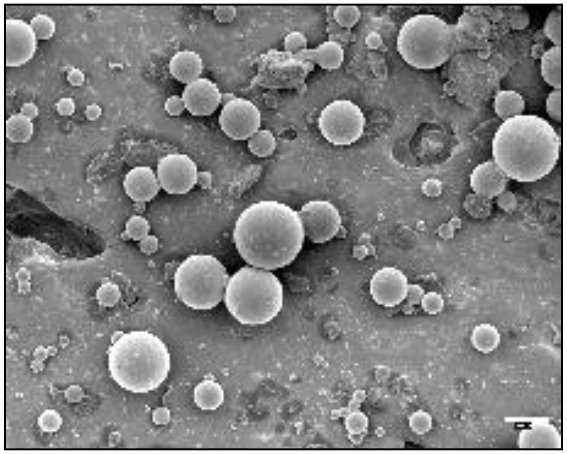
Formulation types and dosage forms and how they are claimed

US201000008961

1. A method for producing a microcapsule, comprising: heating an aqueous dispersion comprising a dispersion stabilizer, an ionic surfactant, a solid biologically active substance, a polymerization initiator and a radical-polymerizable monomer subjected to ultrasonic irradiation.



- Claims focus on the physical form and their production process often without even mentioning any specific compound
- However, formulation types/dosage forms might also be claimed in combination with specific formulation recipes: in this case both aspects of the formulation should be covered by search strategies

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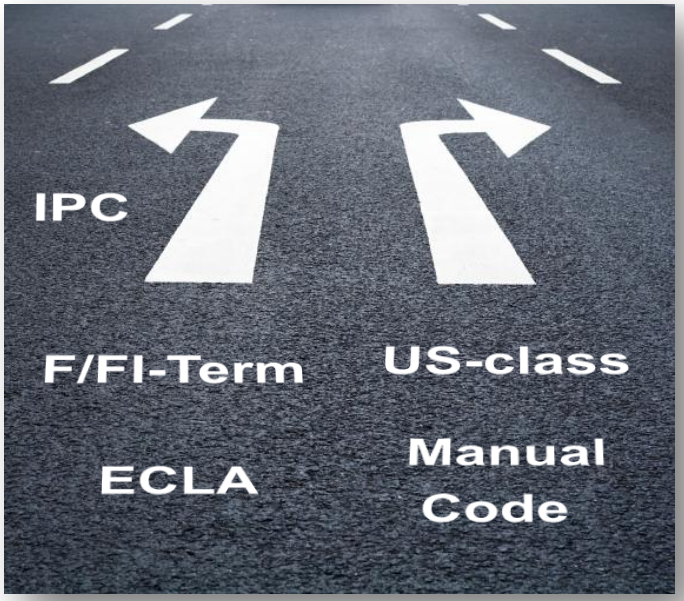
How to search formulation types and dosage forms

- Formulation types and dosage forms are very much concept-based and therefore difficult to search with keywords only
- Codes are crucial to enhance retrieval
- Which codes are to choose?
- Are coding systems at all reliable for comprehensive retrieval of formulations?



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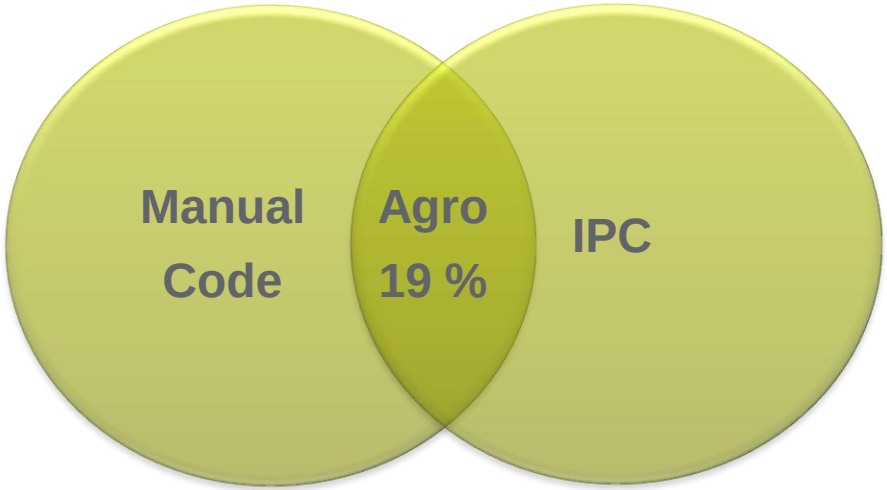
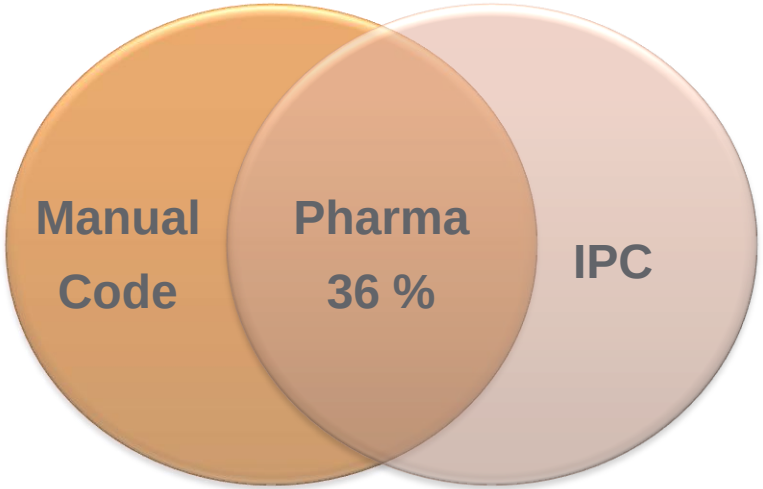
How to search formulation types and dosage forms – database and patent classification codes (1)

C12-M:
Formulation type (agro)



A01N025:
Biocides, etc. characterized by their forms, …

B12-M:
Formulation type (pharma)



A61K009:
Medicinal preparations characterized by special physical form

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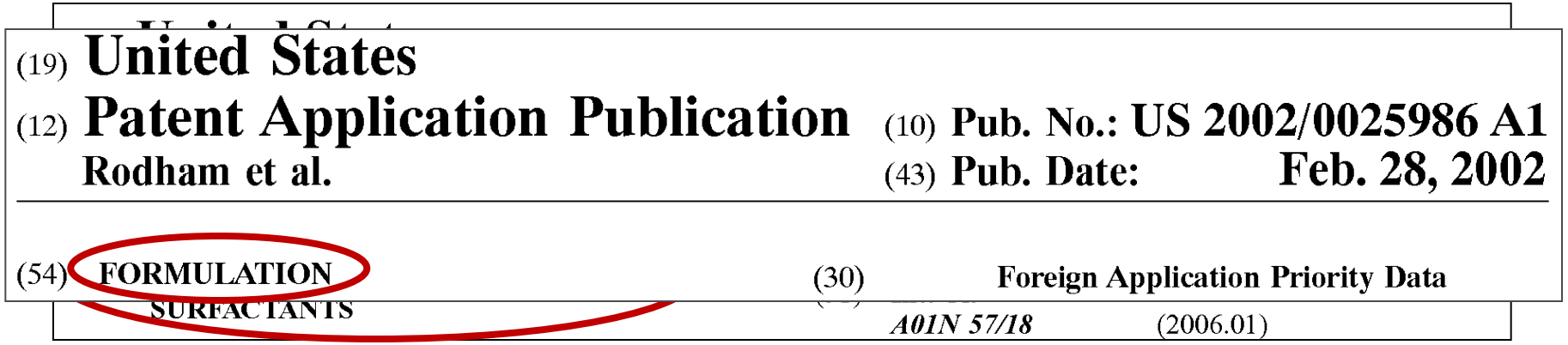
How to search formulation types and dosage forms – database and patent classification codes (2)

- Do not rely on one single coding system, since none of them is exhaustive
- Use as many codes as possible for comprehensive retrieval

	Agrochemistry	Pharmaceuticals
Manual codes (WPIX)	C12-M	B12-M
IPC/ECLA	A01N-025; A01N-017	A61K-009
US-classes	504/358 - 504/367	514/936 - 514/975
F-Terms	4H011/DA; 4H061/FF	4C076/AA; 4C086/MA
FI-Terms	A01N-025	A61K-009

Evaluation and analysis of patent documents – can “informative“ titles help?

- Relevance of documents can often (but not always) already be judged from the title



(19) **United States**

(12) **Patent Application Publication** (10) **Pub. No.: US 2002/0025986 A1**

Rodham et al. (43) **Pub. Date: Feb. 28, 2002**

(54) **FORMULATION**
SURFACTANTS

(30) **Foreign Application Priority Data**

A01N 57/18 (2006.01)

- Recommended to use enhanced titles for evaluation (e.g. from World Patents Index)

ANSWER 1 OF 1 WPIX COPYRIGHT 2010 THOMSON REUTERS on STN
2002-066335 [200209] WPIX
Water-in-oil-water multiple emulsion as slow release formulation, comprises continuous aqueous phase of dispersed oil phase droplets having water-soluble or water-dispersible active material

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Non-patent literature searching – bibliographic databases

- Most bibliographic non-patent literature (NPL) databases support controlled vocabulary and/or codes for chemical formulations
- Examples of bibliographic databases covering **agrochemistry** and **pharmaceuticals**:

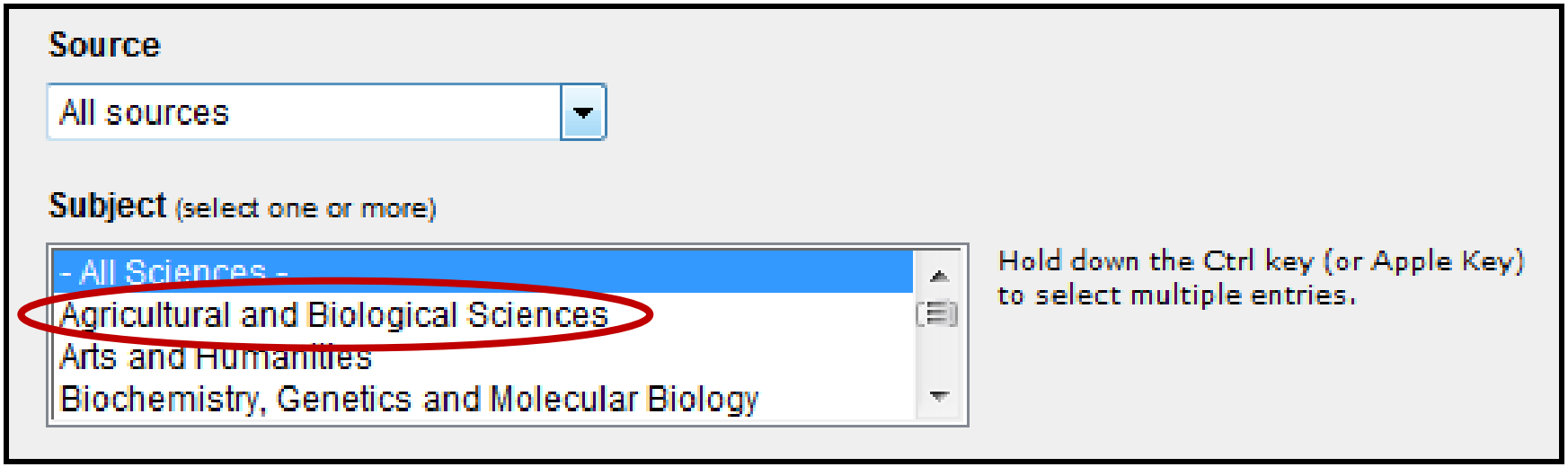
	Controlled terms	Classification codes/MeSH
CA	Agrochemical formulations/CT Pesticide formulations/CT Drug Delivery Systems/CT plus narrower terms (+NT)	**None** **63-6/CC:** pharmaceuticals, formulations and compounding
CABA (agro)	Formulations/CT Application methods/CT both plus narrower terms (+NT)	**HH420/CC:** Chemistry and Formulation
Medline (pharma)	Dosage Forms/CT plus narrower terms (+NT)	**D26.255./CT, D27.720.280./CT, E5.916.250./CT:** Dosage Forms

Non-patent literature searching – full-text searching of E-publications (1)

- “Hidden“ prior art is often insufficiently indexed in bibliographic databases
- Full-text access to non-patent literature is crucial to identify “hidden“ prior art
- Full-text search sites for E-publications (e.g. E-journal search sites) are an important source of non-patent literature prior art (e.g. journals, books, theses, meeting reports, etc.)

No in-depth indexing of formulations and other specific uses provided by major E-publication search sites

Non-patent literature searching – full-text searching of E-publications (2)



www.sciencedirect.com

More sophisticated coding systems for E-publications urgently needed!

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Formulation searching on the Internet

- The internet provides an enormous amount of chemical information, which is often not covered by commercial databases or E-publication search sites
- Chemical information is often represented by chemical structures and formulas and therefore difficult to search with pure keyword strategies
- In patent literature databases coding systems are available linking structural chemical information to specific (formulation) uses, e.g. Derwent Chemical Coding (formulation codes discontinued in 1981) and Derwent Polymer Coding

Is there such thing for searching the internet? NO, but...

Formulation searching on the internet – InChI (IUPAC International Chemical Identifier) (1)

- Developed by IUPAC and NIST during 2000-2005

- Non-proprietary, unambiguous identifier that can be computed from structural information
- Already supported by some databases and scientific journals on the internet and precisely indexed by internet search engines
- Further enhancements planned, e.g. representation of Markush structures, mixtures and polymers
- Value critically dependent on the use of InChI by authors/publishers of internet content

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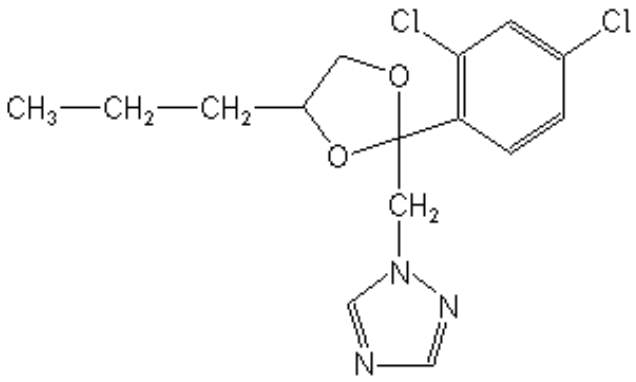
Formulation searching on the internet – InChI (IUPAC International Chemical Identifier) (2)



InChI=1S/C15H17Cl2N3O2/c1-2-3-12-7-21-15(22-12,8-20-10-18-9-19-20)13-5-4-11(16)6-14(13)17/h4-6,9-10,12H,2-3,7-8H2,1H3

Principally „use-layers“ could be introduced to InChI coding to link structural information to specific uses, e.g. in formulations!

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