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An Overview of Biomedical Ontologies for Pandemics and Infectious Diseases Representation

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Abstract

Several infectious diseases and pandemics have so far emerged. Pandemics are by nature rapidly evolving. In this context, COVID-19 cases, seen recently in a growing number of countries around the world, have been increasing exponentially. So, researchers and responsible actors should take quick decisions to mitigate the spread of such diseases. To do so, several computer science solutions, including ontologies, have been proposed to cope with these issues and save humanity. The ontology is the key formalism which allows modelling knowledge along with its semantics in a formal way. Indeed, the ontology provides unambiguous definitions of a discourse's domain terms in a machine understandable way. Particularly, biomedical ontologies have ever been developed to capture and represent pandemics and infectious diseases. In this context, this paper aims to scrutinize and study these state-of-the-art ontologies.

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1. Introduction

The literature [1][2][3] has provided a plethora of ontology definitions. Nonetheless, all these definitions concur that the ontology is the key conceptualization specification which allows modelling knowledge along with its semantics in a formal way. Based on the conceptualization subject, Guarino [4] distinguishes four main ontology

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types, namely high-level, domain, task and application ontologies. High-level ontologies are also known as meta-ontologies, generic or upper-level ontologies. They consist of generic concepts (e.g. time, space, event, etc) which make these ontologies valid for different domains. Domain ontologies are sub-types of high-level ontologies as they model knowledge related to a particular domain (e.g. health, education, etc). Task ontologies model knowledge related to a particular task (e.g. scheduling), regardless of a given domain. Application ontologies are used in a particular task related to a specific domain.

Regardless of the ontology type, the ontology fosters the communication among human beings, human beings and machines or among machines. Indeed, the ontology provides unambiguous definitions of a discourse's domain terms in a machine understandable way. This helps to share knowledge and to reduce any misunderstanding about its details. We can touch this usefulness in the field of infectious diseases and pandemics such as Influenza, Malaria and COVID-19. These are diseases that are more dangerous and contagious than other ones. Indeed, these diseases cause more human and economic damages. By 12 May 2021, the World Health Organization (WHO) reported 159,319,384 confirmed cases of COVID-19, including 3,311,780 deaths. Regarding the economic level, such pandemics affect several sectors such as the tourism and the air travel ones.

Particularly, biomedical applications ontologies have ever been developed to capture and represent pandemics and infectious diseases. In this context, this paper aims to scrutinize these state-of-the-art ontologies.

The remaining of this paper is structured as follows. Section 2 focuses on the background of this survey by describing scientific details about epidemiology and by depicting the ontology lifecycle. Section 3 sheds light on state-of-the-art ontologies of infectious diseases and pandemics. Particularly, Section 4 exposes the state-of-the-art ontologies of coronavirus diseases. Before concluding, Section 5 discusses the literature work.

2. Background

This section presents some emerging pandemics over the time. Moreover, it describes the epidemiologic triangle that helps to understand a given pandemic. Next, this section depicts the ontology lifecycle involved in an ontology engineering activity.

2.1. Pandemics and infectious diseases

Several infectious diseases and pandemics have so far appeared at different dates and in several countries. They are mainly produced by infectious viruses. These diseases are characterized by specific symptoms that allow doctors to identify the disease name. To cope with these diseases, researchers and health agents have produced either vaccines or recommended some general hygiene practices. Table 1 depicts the aforementioned details pertaining to four emerging pandemics over the time, such as Middle East Respiratory Syndrome (MERS) and COVID-19.

Table 1. Details about some pandemics, according to WHO (i.e. World Health Organization) and [5].

Disease	Date	Place	Virus	Symptoms	treatment
Spanish flu or influenza A	1918.	United States.	H1N1 virus.	Fever, cough, sore throat, runny or stuffy nose, headache, muscle aches and fatigue.	Vaccines.
Severe Acute Respiratory Syndrome (SARS)	November 2002	South China	SARS-CoV	Fever, chills, rigors, headache, malaise, muscle pain, onset of a dry, non-productive cough, shortness of breath and hypoxemia.	Quarantine, general hygiene measures such as washing hand and using alcohol-based disinfectants.
MERS	September 2012	Saudi Arabia	MERS-CoV	Fever, cough and shortness of breath. Pneumonia diarrhoea, respiratory failure	Practicing general hygiene measures when being in contact with camels and other animals, quarantine.
COVID-19	December 2019	Wuhan, China	SARS-CoV-2	Fever, dry cough, tiredness, aches, pains. Sore throat. Diarrhoea, headache, loss of taste or smell. A rash on skin. Breathing difficulty, chest pain or pressure.	Washing hands with water and soap or cleaning hand with alcohol-based disinfectants, social distancing, avoiding face touching, quarantine, vaccines.

The CDC †(i.e. Centers for Disease Control and prevention) proposes the epidemiologic triangle to model and understand the main factors of infectious diseases, i.e. their causes and transmission modes. The triangle is a simple model which is made up of three main related nodes, i.e. agent, host and environment (see Fig.1).

- **The Agent** answers the question “what causes the infectious disease?”. It can be a microorganism, a pathogen, a virus, a bacterium, a parasite, or other microbes. SARS-CoV and SARS-CoV-2 are examples of such agents.
- **The host** is the organism which answers the question “who can be infected by a disease agent?”. It can be a human or an animal.
- **The environment** consists in surrounding or external conditions of the host. It answers the question “where the agent finds a favorable environment to be transmitted to the host?”. A dirty water, a blood or even a season of the year may be such an environment.

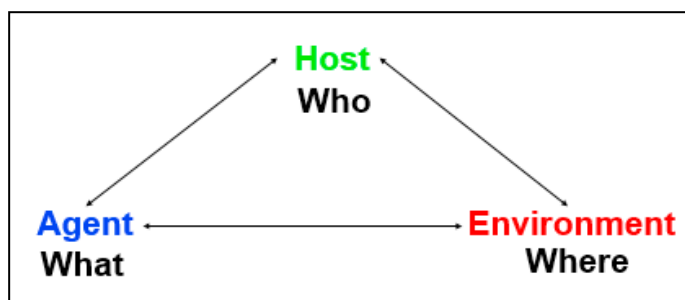


Fig. 1. The epidemiologic triangle.

2.2. Ontology lifecycle

Ontology engineering consists of the activities involved in the ontology development process and in its lifecycle; and the methodologies, tools, and languages that are used to build ontologies [6]. This section presents the ontology lifecycle.

Several state-of-the-art methodologies for ontology development have so far been proposed [7]. They are mainly based on various ontology lifecycles. In what follows, Fig. 2 depicts the ontology lifecycle which includes the most important steps identified in [8], [9], and [10]. They are as follows:

- **Identification and Specification of Needs** have as a purpose identifying users and their needs. To this end, motivating scenarios and/or competency questions have to be conducted, to justify the development or the evolution of an ontology. Then, an informal textual document has to be prepared to describe the identified needs.
- **Conceptualization** consists in representing a domain knowledge along an ontology structure, that is, using concepts, properties, relations and axioms. The output of this stage may be a graph made up of vertices and edges.
- **Formalization** consists in representing the ontology knowledge using a semi-formal language, such as Description Logic (DL) or the Unified Modelling Language (UML).
- **Implementation** consists in formalizing knowledge in a semantic web ontology language using an ontology editor such as Protégé [11].
- **Maintenance** consists in checking the quality of ontology and adapting it to the new emerging requirements. It is often initiated by an evaluation and followed by a change activity such as the evolution one.
 - **Evaluation** consists in the verification of the ontology quality with regard to some predefined criteria, such as consistency and usage. For more details about this activity and these evaluation criteria, we refer the reader to [6] and [12].
 - **Evolution** consists in applying changes to an ontology to reflect new emerging needs [13][14][15].

† <https://www.cdc.gov/csels/dsepd/ss1978/lesson1/>

- **Diffusion and Use** are the activities that follow the ontology building and its maintenance. They refer to the ontology deployment and its use.

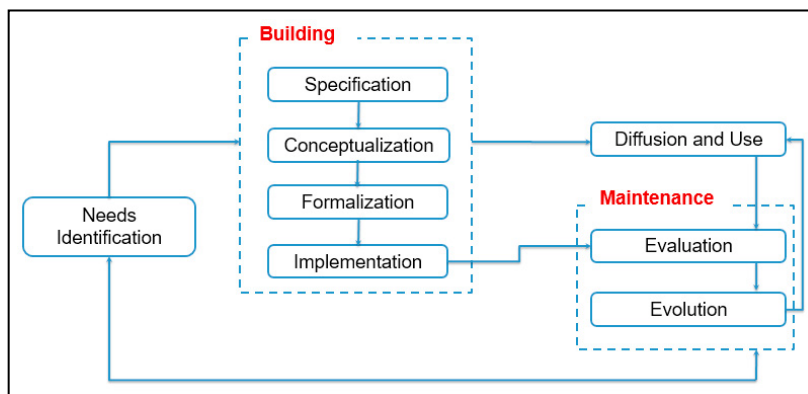


Fig. 2. The ontology lifecycle.

3. State of the art ontologies for earlier infectious diseases representation

In the literature, several ontologies have been developed in the medical domain. For example, Messaoudi et al. [16] proposed an ontology based-approach for diagnosing the hepatocellular carcinoma (HCC) which is a liver cancer tumour. Moreover, Sbissi et al. [17] developed an ontology for the cardiovascular disease.

In our work, we are mainly interested in infectious diseases that are more dangerous and contagious. They also cause more human and economic damages than other diseases. The remaining of this section scrutinizes the state-of-the-art ontologies that have been developed for modeling earlier pandemics and infectious diseases.

In [18], the authors developed a multilingual ontology for the surveillance of infectious diseases such as the avian H5N1 epidemic. This ontology supports their surveillance system for text mining from Internet news and other online sources in several languages.

By the appearance of the malaria disease, the authors [19] developed the IDOMAL ontology using the OBOEdit2 software [20] and following the main principles of the OBO Foundry consortium [21]. IDOMAL extends the Infectious Disease Ontology (IDO-Core) [22] and uses the Basic Formal Ontology (BFO) [23] as an upper-level ontology. The malaria ontology models clinical, epidemiological and vector biology aspects. Later on, the authors applied several revisions on this ontology and reported them in [24]. One of these revisions consists in transforming the IDOMAL ontology from the OBO format to the OWL language [25].

Conway et al. [26] developed a bio-surveillance application ontology for Influenza-Like-Illness (ILI). The ILI ontology was intended for text mining of clinical documents such as emergency room clinical reports.

To model the Brucellosis disease, Lin et al. [27] developed the IDOBRU ontology. Brucellosis is a zoonotic infectious disease caused by intracellular Gram-negative bacteria *Brucella* sup. This ontology extends the core Infectious Disease Ontology (IDO-Core) [22]. Particularly, the IDOBRU ontology models different aspects related to the Brucellosis disease such as host infection, pathogen transmission, symptoms, virulence factors, pathogenesis, diagnosis and epidemiology aspect of Brucellosis, intentional release, vaccine prevention and treatment. To answer queries on the IDOBRU ontology, the authors used the Protégé [11] plugin “DL query tab” and they developed an IDOBRU SPARQL query interface. These tools are used to implement several queries such as “*What Brucella virulence factors are also protective antigens?*”.

To describe the dengue fever, Mitraka et al. [28] developed the IDODEN ontology. Indeed, IDODEN models different aspects of this vector-borne disease such as biology, epidemiology and clinical features. It also models the different facets of dengue entomology considering that mosquitos are which transmit this disease. This ontology extends the IDO ontology and uses the Basic Formal ontology (BFO) as an upper-level ontology. It also reuses other biomedical ontologies and controlled vocabularies.

Camara et al. [29] proposed the Infectious Disease Ontology for SCHISTOsomiasis: IDOSHISTO. This ontology models the schistosomiasis (or bilharzia) disease, according to an abstraction-layered modularization made up of the foundational layer, the core layer and the domain specific layer. The core layer reuses the concepts and relationships of the IDO-Core [22]. The foundational layer is directed by the Basic Formal ontology (BFO) [30]. Regarding the domain specific layer, a module-based approach was adopted to represent epidemiological, biological and clinical perspectives. These perspectives' concepts are related using inter-perspective relations, whereas intra-perspective relations are used to relate the concepts of a given perspective. The IDOSCHISTO ontology was used to annotate and query epidemiological data that are collected within the Richard Toll area in Senegal.

In [31], the authors developed an ontology-based framework for formulating spatial-temporal Influenza (Flu) outbreaks from Twitter, within Ohio. To do so, a web-based tool was developed. It allows visualizing the spatial-temporal influenza spread in the aforementioned city (i.e. Ohio).

Béré et al. [32] developed an extension of the Infectious Disease Ontology for MENingitis (IDOMEN). This ontology models three main perspectives of the meningitis disease, namely biological perspective, clinical perspective, epidemiological and public health perspective. IDOMEN is intended for extracting data from social media texts. It also helps to share and communicate domain knowledge among responsible agents of an epidemiological surveillance system. The authors evaluated their ontology by running queries such as “*Which are the infectious agent carriers that also are Neisseria Meningitidis hosts?*”.

In [33], Radhika et al. developed the swine flu disease ontology to model the novel H1N1 disease (i.e. Hemagglutinin type 1, Neuraminidase type 1). This ontology was developed as follows. First, the authors determined the scope of this ontology. Second, they identified candidate terms. Third, they defined classes taxonomy. Fourth, they established relationships among terms. Finally, they added annotations. To implement this ontology, the authors used the Protégé 4.1 Beta Software. To evaluate this ontology, they used the Fact++ reasoner to run DL queries on this ontology.

4. State of the art ontologies for coronavirus diseases representation

By the emergence of COVID-19, several works have been done. In this context, Lusignan et al. [34] developed an application ontology that is intended for various use-case domains of the RCGP (i.e. Oxford Royal College of General Practitioners RSC (i.e. Research and Surveillance Centre)). More specifically, these use-case domains include primary care, public health, virology, clinical research, and clinical informatics (i.e. the COVID-19 ontology creation). The ontology is also used for surveillance activities of the COVID-19 pandemic. This application ontology was developed in three stages, namely creating and testing a use case, developing the COVID-19 surveillance ontology and external validation using a rapid Delphi consensus exercise. The developed ontology models different aspects such as demographic details, key clinical features, relevant comorbidities, risk factors and mortality. It was developed using the Protégé ontology editor [11] and the Web Ontology Language (OWL) [25].

Moreover, Sargsyan et al. [35] developed the COVID-19 ontology to capture different aspects of the COVID-19 disease such as epidemiology (e.g. risk factors, transmission, etc), clinical aspects (e.g. signs, symptoms, diagnostics and medical intervention), prevention and control, clinical trials, genetic and molecular processes. The COVID-19 ontology is used for text mining approaches and semantic interoperability in the COVID-19 domain. The developed ontology includes 2121 terms imported from existing ontologies and 149 newly defined terms.

Furthermore, Dutta and DeBellis [36] developed another COVID-19 Ontology for cases and patients information (CODO). This ontology was developed to be used by data and services, to model and annotate the COVID-19 information. CODO also aims at developing and offering distributed, heterogeneous, semantic services and applications such as decision support systems and advanced analytics.

The CODO ontology was developed using a nine-step approach, namely definition of purpose, derivation of competency questions, term extraction, analysis, knowledge synthesis, reuse and standardization, design of a representational model, ontology development and evaluation.

The representational model captures information about COVID-19 cases (i.e. recovered cases, available resources and requirements, etc) and COVID-19 patient data (i.e. inter-personal relationships between patients, suspected transmission reasons, tracking of patient test results, etc). For example, the relationship “*suspectedReasonOfCatchingCovid-19*” is used to model the main potential reasons behind catching the COVID-19

disease. The domain of this relationship is the class “*Patient*”, and its range is the class “*ExposureToCOVID-19*”. To model the potential causes of catching COVID-19, the authors identified several sub-classes of the class “*ExposureToCOVID-19*” such as “*CloseContact*”, “*ContactWithHealthWorkers*”, “*ExposureViaGathering*”, “*InfectedFamilyMember*”, “*InfectedViaJob*”, etc.

More specifically, the ontology development step is directed by the Protégé ontology editor [11] and the OWL language [25].

To evaluate the CODO ontology, the authors imported data from the government of India using the Cellfie plugin [37]. They also ran SPARQL DL queries using both the Pellet reasoner [38] and the snap SPARQL plugin of Protégé [39]. Moreover, the authors exported the CODO ontology into the AllegroGraph triple store [40].

SPARQL queries are used for example to “*find all People who have a close relation to someone who has been diagnosed with Covid and who has not yet been tested*”, “*show the patients with the possible reasons of catching COVID-19. Also, display the relationships between the patients, if any*” and “*show the travel history of a patient p*”.

Recently, He et al. [41] developed the Coronavirus Infectious Disease Ontology (CIDO). This ontology models different aspects of coronavirus diseases such as etiology, transmission, epidemiology, pathogenesis, diagnosis, prevention and treatment. CIDO is a community-driven ontology which extends the Infectious Disease Ontology and imports several terms from about 20 state-of-the-art ontologies such as Chemical Entities of Biological Interest ontology (ChEBI) [42], Human Phenotype Ontology (HPO) [43], Disease Ontology (DO) [44] and the NCBI taxonomy ontology (NCBITaxon) [45]. The same authors extended their work in [46] to focus on the drugs modelling. Indeed, they identified over 130 chemical drugs and antibodies against infection of human coronavirus from the biomedical literature. Then, the authors plan to annotate these results into the CIDO ontology.

5. Synthesis and open challenges

Table 2 depicts a comparison among the prevalent state-of-the-art biomedical ontologies that have been described in both Section 3 and Section 4.

The described ontologies are application ontologies considering that they model a specific task of the medical domain. Indeed, these ontologies have been created to model several aspects of infectious diseases and pandemics. Nonetheless, most of them have covered epidemiological, clinical and biology aspects of such diseases. Interestingly, these biomedical ontologies have been developed synchronously with the appearance of the described diseases.

Most of pandemics ontologies extend the IDO core ontology. They are also based on the Basic Formal ontology (BFO) which is an upper-level ontology. The state-of-the-art ontologies reuse other biomedical ontologies such as the Ontology for General Medical Science (OGMS) [47], the Ontology for Biomedical Investigations (OBI) [48], the Vaccine Ontology (VO) [49], The Human Phenotype Ontology (HPO) [43] and the Chemical Entities of Biological Interest ontology (ChEBI) [42]. Infectious diseases ontologies reuse also other non-biomedical ontologies such as the Friend of a Friend ontology (FOAF) [50]. This reuse allows an interoperability among the different ontologies.

To develop pandemics ontologies, several tools have been used. These tools were used to support ontology developers along some steps of the ontology lifecycle. In what follows, we outline some of them:

Protégé Desktop [11] is used for the “implementation” step in the ontology lifecycle (See Section 2.2). It is developed in the Java language on top of the OWL API [51]. It is compliant with the semantic web and W3C standards. This editor offers a basis of functionalities for constructing, loading and editing OWL 2 ontologies in different syntaxes. Thanks to its plugin-based architecture that extends its functionality, various plugins are installed and integrated by default in the downloaded version.

For the “evaluation” step in the ontology lifecycle, several tools have been used such as Snap-SPARQL Query Plugin, DL Query Tab, reasoners, OOPS and AllegroGraph.

Snap-SPARQL Query Plugin [39] is an open source Protégé plugin which allows users to query an OWL ontology while taking into consideration inferred knowledge. The query language supported by this plugin is SPARQL 1.1 (SPARQL Protocol And RDF Query Language) [52]. It is mainly distinguished from its anterior version SPARQL 1.0 by its support to OWL entailment regimes [53] rather than only the simple entailment regime.

DL Query Tab is an open source Protégé plugin for querying an OWL ontology about direct/indirect subclasses/super-classes or instances of a class expression which is written in the Manchester syntax.

Reasoners or inference engines are programs that deduce logical consequences from a set of axioms which are explicitly declared in an ontology. It is commonly used to provide some reasoning services, such as consistency and entailment. Hermit [54] and Fact++ [55] are examples of such reasoners.

OOPS [12] (Ontology Pitfall Scanner!) is a tool which validates an ontology with regard to some predefined pitfalls such as logical inconsistency and some style issues.

AllegroGraph [40] is a graph database and a commercial triple store which allows storing and querying RDF data.

For the “diffusion and use” steps, several websites have been used to publish the developed pandemics ontologies. For example, the BioPortal, OBO Foundry and GitHub websites. These websites promote the reuse and extension of these ontologies.

It is undoubtedly that some ontologies (e.g. [34]) have undergone a rigorous evaluation process. Nonetheless, most of them (e.g. [27] and [41]) have been evaluated using just DL (i.e. Description Logic) queries that are based on some predefined competency questions. Therefore, it is interesting that the developed ontologies undergo an extensive evaluation to enhance their use.

To conclude, developing biomedical ontologies allows the health domain actors to share and communicate consensual knowledge about infectious diseases. This promotes the surveillance of pandemics and mitigates their spread. However, these ontologies model a specific disease or pandemic. What is lacking most is an ontology that models more than one disease, especially when these diseases are similar in terms of symptoms or biological aspects. This helps to share knowledge and to reduce any misunderstanding about infectious diseases details. Furthermore, this missing ontology helps to release new vaccines and drugs for emerging pandemics.

Table 2. Comparison among biomedical ontologies for pandemics representation.

Work	Ontology and Disease nouns	Modelled aspects	Reused ontologies	Languages /Tools	Evaluation approach	Design goals
[19][24]	IDOMAL Malaria	Clinical, epidemiological and vector biology aspects.	IDO core, BFO, and other biomedical ontologies	OBOEdit2 software. OBO format. OWL.	-	Using this ontology by IT tools to control malaria.
[27]	IDOBRU Brucellosis	Host infection, symptoms, pathogenesis, diagnosis epidemiology prevention and treatment.	IDO Core 10 other ontologies	Protégé 4, DL query tab. Developing an IDOBRU SPARQL query interface.	DL queries	Supporting data Interoperability and reasoning.
[28]	IDODEN dengue fever	Biology, epidemiology and clinical features. The different facets of dengue entomology.	IDO core, BFO, IDOMAL, and other biomedical ontologies	OWLtoOBO software. Protégé. OWL. OBO.	-	The annotation of dengue-related data. The construction of decision support systems.
[29]	IDOSCHISTO schistosomiasis (or bilharzia)	Epidemiological, biological and clinical perspectives.	IDO core, BFO and other ontologies.	Protégé OWL.	Querying epidemiological data. State-of-the-art evaluation tools.	Annotating pandemic data and monitoring the disease spread.

[32]	IDOMEN Meningitis	Biological perspective, clinical perspective, epidemiological and public health perspective.	IDO core, OGMS, OBI and NCBI Taxonomy.	The reasoner FaCT++ 1.6.5, Protégé, OWL 2.	Running queries	Sharing domain knowledge among responsible agents
[34]	The COVID-19 Surveillance Ontology	Demographic details, key clinical features, relevant comorbidities, risk factors and mortality.	SNOMED CT	Protégé, OWL.	Various use-case domains of the RCGP RSC. External validation using a rapid Delphi consensus exercise	Surveillance activities of the COVID-19 pandemic.
[36]	CODO COVID-19	Cases and patients information, relations, geographic locations, and date-time information.	SNOMED CT FOAF	OWL DL Protégé, the pellet reasoner, SWRLTab, Cellfie, snap SPARQL, AllegroGraph and Allegro's Gruff.	Importing data on the pandemic from the government of India. Querying the ontology. Storing the ontology in a commercial triple store.	Using this ontology by data and services to model and annotate the COVID-19 information. Developing and offering distributed, heterogeneous, semantic services and applications
[41] [46]	CIDO Coronavirus diseases	Epidemiology, pathogenesis, diagnosis and treatment.	IDO Core and other ontologies	Protégé OWL	DL queries	Identifying chemical drugs and antibodies against infection of human coronavirus.

6. Conclusion

This paper has highlighted the importance of biomedical application ontologies in pandemics and infectious diseases representation. Indeed, such ontologies allow understanding and sharing knowledge about the different aspects of these diseases (e.g. epidemiology, clinical and biology, etc). Furthermore, such ontologies help decision-makers in controlling the pandemic and monitoring the health and social situation. These ontologies allow also health researchers to identify drugs and vaccines pertaining to a given infectious disease. Moreover, this survey encourages ontology community to develop new ontologies, either by extending existing ones or by reusing some parts of them. This survey assists also ontology developers in identifying the main tools, languages that can be used to develop their own ones.

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